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MEDICAL RESEARCH COMMITTEE.

REPORTS

OF THE

CHEMICAL WARFARE MEDICAL COMMITTEE.

No. 17—REPORT ON CASES OF POISONING BY "MUSTARD GAS" (DICHLORETHYL SULPHIDE), WITH SPECIAL REFERENCE TO HISTOLOGICAL CHANGES AND TO ALTERATIONS IN THE LEUCOCYTE COUNT.

December 1918.

In January, 1918, the Director-General, Army Medical Service with the concurrence of the Controller of the Chemical Warfare Department, Ministry of Munitions, appointed a special Committee to prepare reports, based upon information received from all sources at the Chemical Warfare Department, for submission to him with a view to their distribution to those concerned, to make suggestions for further co-ordinated medical investigations that may seem desirable, and to advise him generally in respect of the scientific medical aspects of Chemical Warfare. Present constitution of Committee :—

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(With the co-operation of Lieut.-Colonel C. Gordon Douglas, M.C., M.D., R.A.M.C., and Colonel T. R. Elliott, D.S.O., M.D., F.R.S., in France, and of other corresponding members at Porton and in London, Edinburgh, France and Italy.)

REPORTS ALREADY ISSUED.

No. 1. Notes on the Pathology and Treatment of the Effects of Pulmonary Irritant Gases. (*March*, 1918.)

No. 2. The Histological Effects produced by Gas Poisoning and their Significance. (*April*, 1918.)

No. 3. The Symptoms and Treatment of the late Effects of Gas Poisoning. (*April*, 1918.)

No. 4. Polycythæmia after Gas Poisoning and the Effect of Oxygen Administration in the Treatment of Chronic Cases. (*April*, 1918.)

No. 5. The Reflex Restriction of Respiration after Gas Poisoning. (*April*, 1918.)

No. 6. Investigations into the Reaction of the Blood after Gas Poisoning, and the Results of the Administration of Saline and other Substances. The Effects of Bleeding and of the Injection of Calcium Chloride. (*April*, 1918.)

No. 7. Changes observed in the heart and circulation and the general After-Effects of Irritant Gas Poisoning. (*April*, 1918.)

No. 8. Reports on Fatal Cases of Poisoning. (i) Ethyl iodoacetate.

No. 9. Tissue Changes in Animals produced by Pulmonary Irritant Gases. (*September*, 1918.)

No. 10. The Administration of Oxygen in Irritant Gas Poisoning. (*October*, 1918.)

No. 11. Investigations of Chronic Cases of Gas Poisoning. (*October*, 1918.)

No. 12. Treatment of Patients suffering from "Effort Syndrome" by continuous inhalation of Oxygen. (*October*, 1918.)

No. 13. Bleeding after Poisoning by Pulmonary Irritant Gases, with Appendices. (*November*, 1918.)

No. 14. The Delayed Effects of Phosgene in Rabbits, with special Reference to the Influence of Muscular Contraction. (*November*, 1918.)

No. 15. The Later Effects of Irritant Gas Poisoning. (*November*, 1918.)

No. 16. Report on the Length of Stay in Hospital in the United Kingdom, and the Disposal of Gas Casualties. (*November*, 1918.)

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REPORT ON CASES OF POISONING BY "MUSTARD GAS" (DICHLORETHYL SULPHIDE), WITH SPECIAL REFERENCE TO THE HISTOLOGICAL CHANGES AND TO ALTERATIONS IN THE LEUCOCYTE COUNT.

By Matthew J. Stewart, Leeds.

A.—Introductory.
B.—Clinical and post-mortem summaries, Cases 1 to 10.
C.—Description of the histological changes :—
  1. The respiratory system :—
    (*a*) The respiratory passages.
    (*b*) The lungs.
  2. Other organs.
D.—Résumé of morbid anatomical changes.
E.—Description of the leucocytic changes.
F.—Résumé and discussion of the leucocytic changes.

A.—Introductory.

The material on which this report is based consists of a series of ten fatal cases of poisoning by dichlorethyl sulphide in which a post-mortem examination was made, and a detailed histological investigation of the organs subsequently carried out. All the cases had been subjected to shell gas, but whether this was mustard gas only or a mixture is uncertain. Certainly the gas had no immediate ill-effects, and the clinical and pathological features were those of mustard gas poisoning. All the patients were admitted within 48 hours of gassing, and the length of time which elapsed between gassing and death varied from two to eight days—that is to say, all fall within the category of early fatal cases.

Leucocyte counts and blood-film examinations were made at intervals on six of these cases, and on one very severe case which recovered, while seven slighter cases were also examined. For the differential counts 500 or 1,000 cells were enumerated as a rule, but a smaller number, 100—200, had to suffice where there was marked leucopænia.

The post-mortem examinations were usually made within a few hours of death, in several cases within two or three hours. The material for histological investigation was fixed either in absolute alcohol or in formol-saline, and the stains employed were hæmalum and eosin, hæmatoxylin and eosin, Mallory's acid fuchsin-anilin blue-orange G stain, Weigert's fibrin stain, Gram's stain, and Giemsa's eosin-azur. As a rule alcohol-fixed material was used for all but the ordinary hæmalum or hæmatoxylin staining.

B.—Clinical and Post-mortem Summaries.

In each case definite symptoms commenced only after an interval of several hours—6 to 10 as a rule—although in a few instances the patients complained of tingling of the skin within an hour or two of gassing.

Case 1.

Rfm. E., æt. 31, was gassed on the morning of 10th September. On the evening of the following day he was admitted to No. —— General Hospital in a state of profound collapse, with a temperature of 99·8, respirations 44, and an imperceptible pulse. There was an acute conjunctivitis of moderate severity, and the skin of both thighs, both arms and the whole of the back showed extensive erythema and blistering. A wound of the right forearm, with fracture of the ulna, had been excised and bipped, and appeared healthy.

At 11 a.m. on 12th September, two days after gassing, a differential leucocyte count was made and showed the following result: Total leucocytes 18,000 per cub. mm., polymorphonuclears 16,560 (92 per cent.), eosinophils 0, basophils 0, lymphocytes 1,080 (6 per cent.), large mononuclears 360 (2 per cent.). The great majority of the polymorph leucocytes were of more or less embryonic type, a few frankly mononuclear, many possessing rod shaped and horse shoe shaped nuclei. The red cells appeared normal. Some fluid from an unbroken skin vesicle was, after agitation, removed by aspiration and its cellular content estimated. Total leucocytes 2,000 per cub. mm., polymorphonuclears 1,964 (98·2 per cent.), lymphocytes 20 (1 per cent.), large mononuclears 16 (0·8 per cent.). No bacteria were seen in smears.

Death ensued six hours later, roughly 60 hours from the time of gassing.

Post-mortem Examination (17 *hours after death*).

1. *Respiratory Passages.*—The posterior third of the tongue is swollen and œdematous. The soft palate and uvula are red and inflamed, with a small amount of adherent plastic exudation. Pus can be expressed in considerable quantity from the tonsillar crypts on both sides. The larynx and epiglottis show intense congestion of the mucous membrane, with small shreds of inflammatory exudation all over. The trachea and bronchi are the seat of a very intense membranous inflammation. The mucosa is clothed throughout by a thick, greyish-green layer of inflammatory exudate which strips readily, exposing an acutely inflamed wall beneath. The process extends to the middle and smaller tubes.

2. *Lungs and Pleuræ.*—The lungs are markedly congested throughout. Much thin turbid fluid can be expressed from the smaller bronchi of both lungs, but definite pulmonary œdema is limited to the right upper lobe. The posterior portions of both lower lobes show a definite but early broncho-pneumonia, with some small associated patches of collapse. There are numerous small patches of hæmorrhage in the pleura covering the posterior aspect of both lungs.

3. *Other Organs.*—The bronchial glands are enlarged and acutely congested, and contain several old calcareous foci. The pericardial sac contains a few drachms of clear fluid. A few punctiform hæmorrhages are present on the posterior aspect of the left ventricle The right heart contains a small amount of pale soft thrombus, and there is considerable hæmolytic staining of the endocardium of the right auricle. This, and a large area of necrosis in the liver, are found to be associated with the presence of a large, gram-positive, sporing bacillus, morphologically resembling *B. Welchii.* The capsules of the kidneys are slightly adherent, and on stripping leave a finely granular surface. The renal cortex is somewhat yellow and fatty looking, and both it and the medulla show streaky engorgement. The adrenal cortex is notably lacking in lipoids. The brain on section shows general engorgement of the smaller vessels and possibly a number of fine punctiform hæmorrhages in the white matter.

Case 2.

Rfm. F., æt. 36, was gassed on the morning of 12th October. He also sustained a wound of the foot which was excised and bipped, and a scalp wound which was bipped. On admission to No. —— General Hospital next day there was acute conjunctivitis with chemosis, laryngitis, and extensive vesication of the hands and face. Temperature was 98, pulse 120. Next day, on 14th October, the laryngitis was worse, crepitations were heard all over the lungs, and the patient was extremely ill and very cyanosed. The chemosis had increased and there was general haziness of the corneæ. He died that day at 12.45 p.m., roughly 54 hours after gassing.

Post-mortem Examination (2 *hours after death*).

1. *Respiratory Passages.*—There is an intense acute inflammation of the respiratory passages from the mouth to the lungs. The uvula, soft palate and pharynx are least involved, but the epiglottis is very swollen and œdematous, and is covered by an inflammatory membrane continuous with that on the arytenoid cartilages. A similar membrane is present on both sides of the soft palate, but the tonsils have almost entirely escaped. The interior of the larynx, trachea and bronchi is clothed throughout by a thin inflammatory membrane which strips readily, leaving a quite pale surface beneath.

2. *Lungs and Pleuræ.*—The lungs are slightly congested and very crepitant. The acute membranous bronchitis seems to extend into quite small bronchi, but there is no naked eye evidence of pneumonic consolidation. The visceral pleura shows a few punctiform hæmorrhages on the posterior aspect of both lungs near the root.

3. *Other Organs.*—The bronchial glands are the seat of old calcareous and caseous tubercle. There are no ante-mortem coagula in the heart. Numerous fine punctiform hæmorrhages are present in the epicardial covering of the left auricle and both ventricles. The coronary arteries show a number of yellow patches of early degenerative atheroma. The adrenal cortex is somewhat deficient in lipoids. The kidneys are congested, and the liver presents a somewhat nutmeg appearance.

Case 3.

Pte. J. was gassed on the morning of 12th October, and admitted to No. —— General Hospital two days later. He was then cyanosed, with swollen veins and a dilated right heart. There was much laryngitis and tracheitis, and the throat and chest were very painful. The lungs were full of rhonchi and moist râles, and respiration was very difficult. The eyelids were swollen and œdematous, and there was much conjunctivitis. The only blisters present were on the left thigh and right thumb. Venesection was performed at 1 p.m. and brought considerable relief to the patient's symptoms, but he died the same evening at 10.30, about 66 hours after gassing.

Post-mortem Examination (11 *hours after death*).

1. *Respiratory Passages.*—There is very intense, acute membranous laryngitis, tracheitis and bronchitis. The inflammatory membrane is thick, greenish-yellow, and obviously highly purulent. It is not at all firmly adherent, and in the trachea forms thicker bands over the cartilaginous rings than over the intervening spaces. The epiglottis shows only slight membranous inflammation on its laryngeal aspect. The arytenoids and aryepiglottic folds, especially on the left side, are markedly œdematous. The pharynx, uvula, soft palate and posterior third of the tongue are also œdematous, but show only one or two tiny patches of inflammatory membrane.

2. *Lungs and Pleuræ.*—The membranous inflammation of the bronchial tubes extends downwards to the smallest branches visible to the naked eye, and these appear in very many cases to be completely blocked by exudate. The pulmonary tissue is markedly congested, but there is no evidence of general œdema. A number of small, solid, hæmorrhagic nodules are irregularly scattered

throughout both lower lobes. The right middle lobe is unusually large, and contains several large wedge-shaped masses of early pneumonic consolidation. There is also a good deal of œdema in this lobe. There is an early acute pleurisy over the right lower and middle lobes, with numerous small hæmorrhages up to ⅛ inch diameter on the posterior surface of both lower lobes and on the diaphragmatic aspect of the right.

3. *Other Organs.*—The pericardium contains several drachms of clear yellow fluid. There are some patches of chronic fibrosis of the visceral layer. The spleen is enlarged (14 oz.), and shows irregular congestion. The adrenals contain abundant cortical lipoid, and the yellow and brown layers of the cortex and the grey medulla are very well differentiated. The kidneys are congested, especially the left, and contain three small adrenal rests. The brain on section shows intense vascular engorgement.

Case 4.

Pte. M., æt. 28, was gassed on the morning of 12th October, but did not know how long he was exposed. When he was admitted to No. —— General Hospital the following day his eyes and nose were discharging pus and the chest was full of râles. Next day (14th October) he was dyspnœic, with râles and rhonchi on both sides of the chest. The conjunctivæ were intensely congested and somewhat œdematous, but there was no evidence of skin involvement. By 16th October the patient's condition had become very grave, the temperature was 103, pulse 136, and respirations 44. There were signs of consolidation of the right lung. He died on 17th October at 2.30 a.m., five days after gassing.

Post-mortem Examination (*7 hours after death*).

1. *Respiratory Passages.*—The larynx, trachea and bronchi are the seat of an intense acute membranous inflammation. In the trachea and bronchi the membrane is patchily distributed and separates readily from the subjacent mucosa, which is intensely engorged, with numerous punctiform hæmorrhages. In the larynx there is a thick layer of membrane from the true vocal chords downwards. A similar lesion, but with a thinner and more firmly adherent membrane, is present in the pharynx and on the epiglottis, to a less extent on the palate and uvula. The tonsils and tongue are not involved. There is much vascular injection and swelling of the nasal mucous membrane.

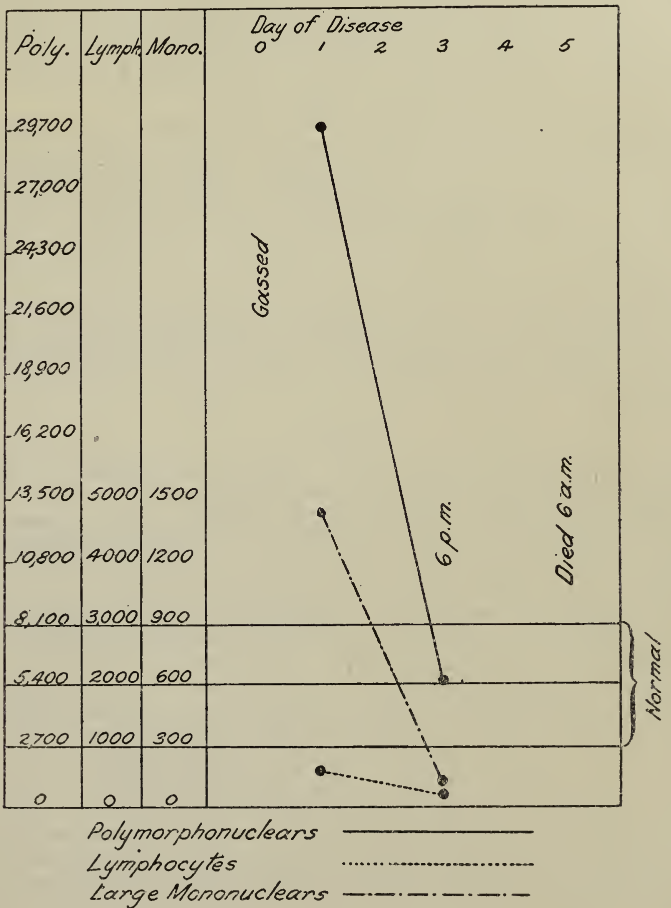
2. *Lungs and Pleuræ.*—The right lung is the seat of patchily distributed pneumonic consolidation, with intervening emphysematous and œdematous areas, and a considerable area of collapse at the extreme base. Much the greater portion of the upper lobe is consolidated, while the process is both earlier and less extensive in the lower lobe. The consolidated areas are reddish-white in colour, and beads of pus exude from the cut surface on pressure. The lesion is clearly broncho-pneumonic. In some of the most advanced patches the lesion is going on to suppurative softening, and this is particularly striking in the apical region. The left lower lobe contains throughout innumerable small patches of consolidation, mostly dark purple in colour with whitish centres; evidently pneumonic patches with a hæmorrhagic zone round about. A similar process is commencing in the adjacent part of the upper lobe. The middle sized and smaller bronchi throughout both lungs are filled with purulent exudate, and membranous inflammation extends downwards as far as the eye can detect. There is an early acute fibrino-purulent pleurisy irregularly distributed over the right lung. On the left side the visceral pleura is the seat of much diffuse ecchymosis. Punctiform hæmorrhages are present at the bases of both lungs.

3. *Other Organs.*—The mediastinal tissues are œdematous, and the pericardium contains several drachms of clear yellow fluid. There are numerous fine punctiform hæmorrhages into the epicardium around the base of the left ventricle. The liver is somewhat yellow and fatty looking. The adrenals show considerable reduction in cortical lipoid. There are a number of ectopic nodules of cortex adjacent to the main gland. The kidney cortex is pale and yellowish, the medulla congested. There is intense engorgement of the small vessels of the brain, and a few tiny points of hæmorrhage. The thyroid is considerably enlarged.

Case 5.

Pte. B., æt. 32, was gassed on 2nd October. Irritation of the skin commenced about an hour after gassing, and blistering was first observed some 8 to 10 hours after. He was asleep, and was probably exposed to the gas for some time. On admission to No. —— General Hospital on 3rd October he was in a very feeble state, with profuse purulent conjunctivitis, and a generally œdematous condition of the face. The skin was red all over, with numerous blisters, especially on the face, arms and legs. The penis, scrotum and perineum were also badly burnt. There was some laryngitis and tracheo-bronchitis, with a few râles, but no dyspnœa. Alkaline inhalations were administered. A leucocyte count at 6.45 on the evening of admission (about 36 hours after gassing) showed: Total leucocytes 32,000 per cub. mm., polymorphonuclears 29,860 (93·3 per cent.), eosinophils 0, basophils 0, lymphocytes 700 (2·2 per cent.), large mononuclears 1,440 (4·5 per cent.). A leucocyte count on some of the vesicle fluid, removed by aspiration after agitation, showed: Total leucocytes 1,200 per cub. mm., polymorphonuclears 1,186 (98·8 per cent.), lymphocytes 10 (0·8 per cent.), large mononuclears 2 (0·2 per cent.), tissue cells 2 (0·2 per cent.). No bacteria were seen in smears. On 5th October, three days after gassing, there was much dyspnœa with expectoration of large quantities of mucopus. Cyanosis was present in an extreme degree. A leucocyte count at 6 p.m. showed total leucocytes

CHART 1.—*Case* 5. Pte. B.



6,000 per cub. mm., polymorphonuclears 5,640 (94 per cent.), lymphocytes 240 (4 per cent.), large mononuclears 120 (2 per cent.). The patient died at 6 p.m. on 7th October, five days after gassing.

Post-mortem Examination (4 *hours after death*).

1. *Respiratory Passages.*—The tongue shows considerable swelling and injection of the circumvallate papillæ and posterior third generally. The tonsils are injected, with a small amount of adherent membrane. The palate and uvula show early membranous inflammation. The pharynx, epiglottis, larynx, trachea and bronchi are the seat of an intense acute membranous inflammation, the mucosa being covered by a thick greenish-yellow membrane, firmly adherent over the pharynx and epiglottis, easily separable in the larynx, trachea and bronchi. In the two latter situations the membrane is in places ballooned out by blood-stained dropsical effusion between it and the mucous membrane, and there is a great tendency for it to separate spontaneously in consequence. The membrane itself is thicker and more œdematous here than in the pharynx, leading to considerable narrowing of the lumen of the tubes.

2. *Lungs and Pleuræ.*—There is a widespread condition of hæmorrhagic infarction irregularly scattered throughout both lower lobes, especially the left, with some small early broncho-pneumonic foci. The lungs are congested, but there is no obvious œdema. The membranous inflammation of the bronchi extends down to those of middle size at least. There is very early pleurisy at the extreme left base. A number of old dense adhesions are present over the upper third of the left lung.

3. *Other Organs.*—There is an old caseous and calcareous tuberculous lesion of the bronchial glands. All the chambers of the heart, especially the right, contain large, tough, white ante-mortem coagula. The adrenals are slightly deficient in cortical lipoid. The brain on section shows considerable vascular engorgement.

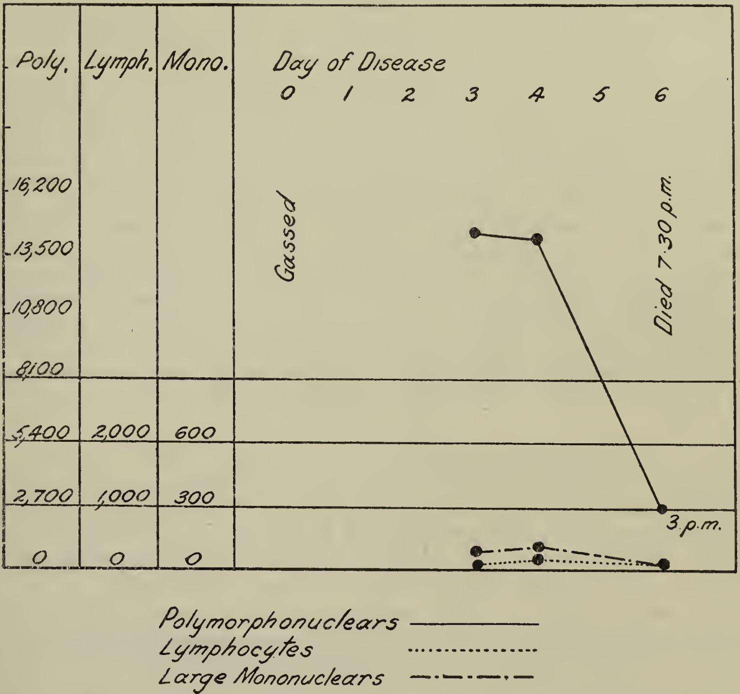
Case 6.

Gnr. B., æt. 45, was gassed on 12th October. On admission to the Field Ambulance some hours later there was cough, retching and vomiting, the eyes were painful and smarting, and the throat was dry. When admitted to the Casualty Clearing Station 24 hours later there were blisters on the right arm and chin, with redness of the forearms. The eyelids were œdematous and there was conjunctivitis. The throat and chest were painful, but there was no cough. A few râles were heard on auscultation. The pulse was 80 and the heart appeared normal. On admission to No. —— General Hospital on 14th October, 48 hours after gassing, there were obvious burns, with blistering of the face and chest. There was severe conjunctivitis with much photophobia and lachrymation, and laryngitis and bronchitis were present. The patient, a stoutish, elderly man, was very feeble and rather blue. On 15th October, when the first blood examination was made, the patient was very ill, with cyanosis, bronchitis and aphonia, and there was copious purulent expectoration and distressing dyspnœa. A leucocyte count at 12.30 p.m. showed total leucocytes 14,500, neutrophil polymorphs 14,370 (99·1 per cent.), eosinophils 0, basophils 0, lymphocytes 70 (0·5 per cent.), large mononuclears 60 (0·4 per cent.). Next day the patient was no better, and there were signs of pneumonic consolidation at both bases. A leucocyte count was made at 4 p.m., four days after gassing. Total leucocytes 14,300, neutrophil polymorphs 14,040 (98·2 per cent.), lymphocytes 170 (1·2 per cent.), large mononuclears 90 (0·6 per cent.). Many of the neutrophils were abnormally large, with six or eight lobes to the nuclei. By 18th October the patient was slightly delirious. He no longer kept his eyes closed, so that cloudiness of the corneæ was very obvious. The dulness at the bases of the lungs had extended well up the scapulæ. Blood examination at 3 p.m. (six days after gassing) showed total leucocytes 2,800, neutrophils 2,670 (95·3 per cent.), lymphocytes 90 (3·4 per cent.), mononuclears 40 (1·3 per cent.). The great majority of the neutrophils were of primitive type, with nuclei of one, two, and three lobes, but a few large polymorphs with nuclei of six and seven lobes were still seen. The patient died the same evening at 7.30, six days after gassing.

Post-mortem Examination (14 *hours after death*).

1. *Respiratory Passages.*—There is very intense membranous inflammation of the interior of the larynx, the epiglottis, and the uppermost inch of the trachea. The membrane is thick, yellow and adherent, and is covered on the surface with much mucopus, which can be washed off. The ventricle of the larynx is filled with similar purulent exudate, but without any underlying membrane. The mucosa over the arytenoid cartilages is very much thickened and œdematous and the seat of numerous punctiform hæmorrhages. The rest of the trachea and the main bronchi show only a small amount of adherent membrane posteriorly. The mucosa in front, covering the cartilaginous rings, is intensely injected and the seat of innumerable tiny punctiform hæmorrhages. The pharynx shows a somewhat patchily distributed membrane stopping short as usual at the commencement of the œsophagus. A few patches of membrane are also present on the uvula and soft palate. The posterior third of the tongue and the pillars of the fauces show considerable œdema.

Chart 2.—*Case* 6. Gnr. B.



2. *Lungs and Pleuræ.*—There is well-marked purulent bronchitis throughout both lungs, some of the tubes being filled with yellow, creamy pus, while others contain more viscid secretion. Early broncho-pneumonia is also present, but is confined to the basal portions of the lower lobes. Both lungs are greatly engorged and somewhat œdematous, the latter change most pronounced in the left upper lobe. There is an extensive old, caseous tuberculous lesion in the apical portion of the right upper lobe. The right pleural sac is completely obliterated by old dense adhesions, in the midst of which are a number of old calcareous plaques. There is an early acute pleurisy over the greater part of the left lung, with a small amount of plastic exudation.

3. *Other Organs.*—The bronchial and tracheal glands are very much enlarged and intensely engorged, while they contain a notable excess of carbon. There are a few punctiform hæmorrhages in the visceral pericardium on the posterior aspect of the heart. Tough, white, ante-mortem coagula of large size are present in all the chambers of the heart. The coronary arteries, especially the left, are

the seat of well-marked patchy atheroma. In particular the descending branch of the left coronary has its calibre very seriously diminished. The cortical lipoid of the adrenals is much reduced, remaining only in patches. The brain and membranes show considerable general vascular engorgement, and there are a number of tiny punctiform hæmorrhages into the ependyma of the lateral ventricles as well as into the white matter of the brain.

Case 7.

Pte. C., æt. 23, was gassed on 12th October, and sustained at the same time a through-and-through wound of the right shoulder and glancing wounds of the left shoulder and left thigh. On admission next day to No. —— C.C.S., there were early burns, with blistering, of the face, trunk and limbs, and early conjunctivitis with chemosis. The heart and lungs were normal. On admission to No. —— General Hospital on 14th October there was much œdema of the right conjunctiva and conjunctivitis of the left, with slight superficial ulceration of the lower parts of the corneæ. There were extensive multiple burns of the face, body, limbs and scrotum, with many bullæ and patches of necrotic epidermis. There was some laryngitis, but no bronchitis, and the respirations were not increased. The temperature was 99·4 degrees, pulse rate 100. A blood examination at 12 noon on 14th October showed total leucocytes 35,000, neutrophil polymorphs 33,810 (96·6 per cent.), eosinophils 0, basophils 0, lymphocytes 530 (1·5 per cent.), large mononuclears 660 (1·9 per cent.). A blood examination at 3.30 p.m. on 15th October showed total leucocytes 16,000, neutrophil polymorphs 15,820 (98·9 per cent.), lymphocytes 80 (0·5 per cent.), large mononuclears 100 (0·6 per cent.). Many of the neutrophils were of very large size, with nuclei of six, seven and eight lobes. On 17th October the patient's condition was much worse. On 18th October he was unconscious ; the pulse was feeble, and the urine scanty, and there was blood-stained vomit. Temperature was 103°, pulse 132, and respirations 20. On 19th October the pulse was uncountable, and the temperature had fallen to 97°. A blood count at 4.40 p.m. showed total leucocytes 200, neutrophil polymorphs 172 (86 per cent.), eosinophils 4 (2 per cent.), basophils 0, lymphocytes 16 (8 per cent.), large mononuclears 8 (4 per cent.). The patient died at 11 p.m., seven days after gassing.

Post-mortem Examination (12 *hours after death*).

1. *External Appearances.*—There is an intense acute conjunctivitis with considerable hæmorrhage into the bulbar portion. There are very extensive burns, with vesication and desquamation, of the greater part of the face, trunk and limbs, penis, scrotum and perineum. The feet alone have completely escaped.

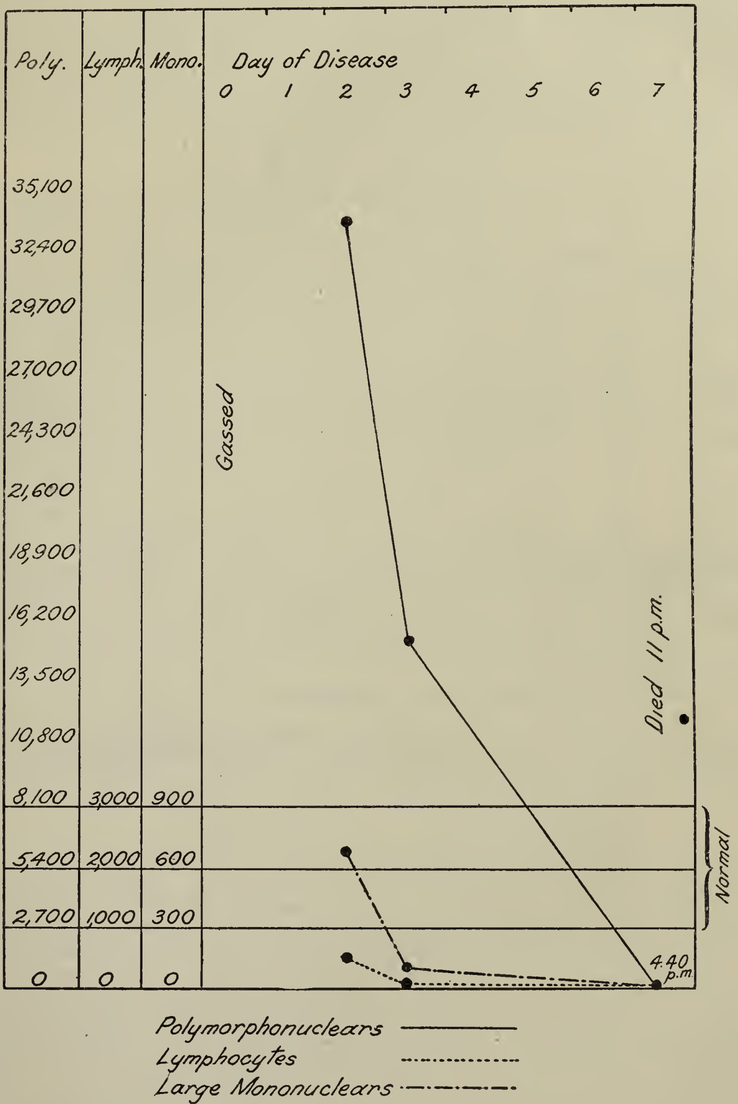
2. *Respiratory Passages.*—A few small, scattered patches of inflammatory membrane are present on the pharynx, tonsils, laryngeal aspect of the epiglottis, and posterior third of the tongue. The larynx and upper half of the trachea appear normal ; the lower half of the trachea and the main bronchi show considerable congestion, and the mucosa is covered by a small amount of purulent material which washes off under a stream of water.

3. *Lungs and Pleuræ.*—The right lower lobe is studded throughout by what are apparently hæmorrhagic infarcts of various sizes, the largest about half an inch in diameter. They are most numerous in the posterior part of the lobe. A similar process in an earlier stage and less extensive is present in the right upper lobe. The middle-sized bronchi contain a small amount of blood-stained mucopus, but no pus exudes from the smaller bronchi, and there is no evidence of bronchopneumonic consolidation. There are numerous irregular patches and spots of hæmorrhage on the posterior surface of the left lung, to a less extent of the right. There is an early pleurisy at the right base with a small amount of plastic exudation.

4. *Other Organs.*—The bronchial glands are considerably enlarged. In the visceral pericardium there are numerous fine punctiform hæmorrhages on the posterior aspect of the left ventricle and along the coronary sulcus. There are

tough, white ante-mortem coagula of small size in both ventricles of the heart. The aorta and coronary arteries show numerous small fatty streaks and patches. The spleen, which is slightly enlarged, is very dark and firm on section. The adrenals are of normal size, but the cortex is notably deficient in lipoids. The liver is the seat of marked cloudy swelling. The stomach contains a large amount of dark green fluid material. Towards the pylorus the mucosa is covered by a thick layer of greenish mucopus, which wipes off with great ease. (A similar condition is found in Case 10.) The subjacent mucosa is not congested. A mesenteric gland in the ileo-colic angle is the seat of an obsolete calcareous tuberculous lesion. The right testis is small and tough, and the tubules when pulled out are small and atrophic.

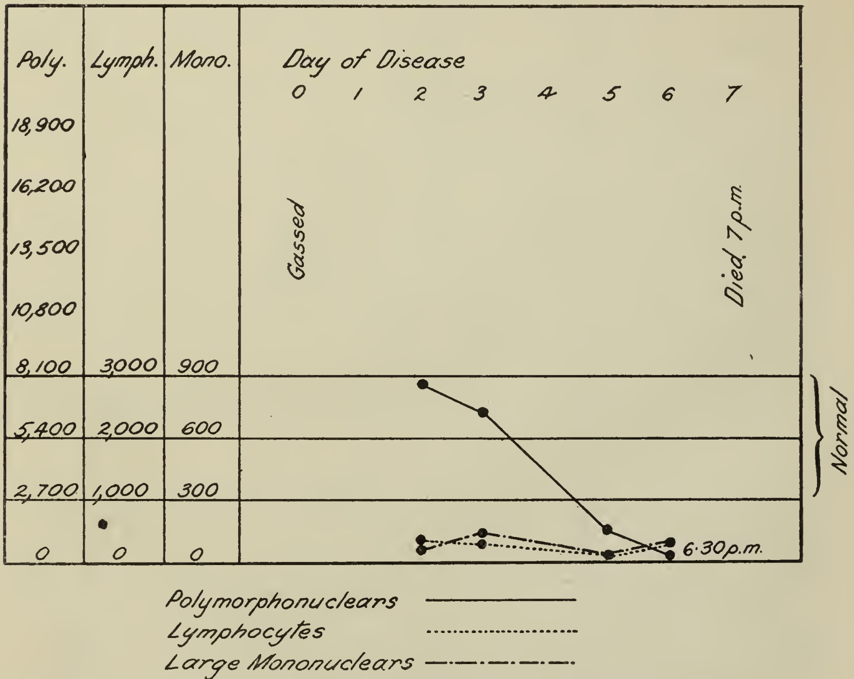
CHART 3.—*Case* 7. Pte. C.



Case 8.

Pte. P. was gassed on 12th October, and admitted the same day to No. —— Field Ambulance with dry cough, vomiting and conjunctivitis. Next day, on admission to No. —— Canadian C.C.S., the temperature was 98° and the pulse 102. The eyes were swollen, there was conjunctivitis, and the throat was sore. On admission to No. —— General Hospital later in the same day there was marked œdema of both conjunctivæ. Next day, 14th October, the patient was cyanosed, dyspnœic and very ill. A leucocyte count at 4 p.m. showed total leucocytes 8,000 per cub. mm., neutrophil polymorphs 7,630 (95·4 per cent.), eosinophils 0, basophils 20 (0·2 per cent.), lymphocytes 290 (3·6 per cent.), and large mononuclears 60 (0·8 per cent.). A leucocyte count at 7 p.m. next day (15th October), showed total leucocytes 7,000, neutrophils 6,650 (93·6 per cent.), eosinophils 40 (0·6 per cent.), basophils 0, lymphocytes 280 (4 per cent.), and large mononuclears 130 (1·8 per cent.). On 16th October the patient's condition was distinctly worse. On 17th October the temperature, which had ranged between 101° and 103° since admission, rose to 104°, and the respirations were 40. The patient was almost aphonic and flushed rather than cyanosed. A leucocyte count at 6 p.m. showed total leucocytes 1,300, neutrophils 1,155 (89 per cent.), eosinophils 5 (0·3 per cent.), basophils 0, lymphocytes 100 (7·5 per cent.), and large mononuclears 40 (3·2 per cent.). Many of the neutrophils were very large, with nuclei of six and seven lobes. On 18th October the patient's condition had become critical. A leucocyte count at 6·30 p.m. showed total leucocytes 500, neutrophils 270 (54 per cent.), eosinophils 0, basophils 0, lymphocytes 170 (34 per cent.), and large mononuclears 60 (12 per cent.). The patient died next day (19th October), at 7 p.m., seven days after gassing.

Chart 4.—*Case* 8, Pte. P.



Post-mortem Examination (*16 hours after death*).

1. *External Appearances.*—There is intense acute conjunctivitis with much hæmorrhage into the bulbar portion and some hæmorrhages into the eyelids. There are a few drying hæmorrhagic vesicles round the mouth.

2. *Respiratory Passages.*—There is very intense acute membranous inflammation of the pharynx, fauces, uvula, soft palate and posterior third of the tongue. The membrane, which is thick, greenish-yellow and adherent, is not universally present, being most abundant on both sides of the epiglottis, on the posterior wall of the pharynx and in the pyriform sinuses. The larynx, trachea and bronchi are similarly and intensely affected, but the membrane is looser and more friable, and is much more easily detached. The subjacent mucosa is very intensely congested.

3. *Lungs and Pleuræ.*—A considerable portion of the left upper lobe is the seat of early broncho-pneumonic consolidation, the intervening lung tissue being markedly œdematous. Both lower lobes show a condition of patchily distributed early hæmorrhagic infarction, with again marked œdema of the intervening lung tissue. The bronchial tubes down to the smallest visible to the naked eye contain inflammatory exudate, and in the middle-sized tubes at any rate there is a definite membrane. There are a few old plural adhesions and a commencing recent pleurisy on both sides, with numerous irregular hæmorrhages on the posterior aspect of the lungs.

4. *Other Organs.*—The bronchial, tracheal and cervical glands are much enlarged and congested, especially the former, which constitute a mass as large as a pigeon's egg. A number of punctiform hæmorrhages are present on the posterior aspect of the heart. All four chambers contain tough, white, antemortem coagula. The spleen, which is somewhat enlarged, is very dark and firm on section. The adrenal cortex is notably lacking in lipoids. The liver is deeply scarred on the surface, with capsular thickening and adhesions, especially over the left lobe. The thickening of Glisson's capsule extends deeply into the parenchyma of the organ. The kidneys are much congested, as is also the gastric mucosa.

Case 9.

Pte. D. was gassed on 12th October, and admitted to No. —— General Hospital two days later. He had then acute conjunctivitis, and an acute dermatitis of the penis, scrotum and perineum. Acute bronchitis, present from admission, developed after some days into a gangrenous condition, with profuse fœtid expectoration. Broncho-pneumonia appeared as a terminal event, and death took place at 5 p.m. on 20th October, eight days after gassing.

Post-mortem Examination (17 *hours after death*).

1. *External Appearances.*—There is well-marked conjunctivitis and superficial keratitis, with inflammation of the eyelids. There are a few patches of superficial dermatitis around the mouth and nostrils, and a similar but more advanced lesion is present on the penis, scrotum and perineum.

2. *Respiratory Passages.*—There is an acute membranous inflammation of the pharynx, uvula and soft palate, the membrane being scanty and patchy, but firmly adherent. As usual the inflammatory process does not extend into the œsophagus. The larynx, trachea and bronchi are lined throughout by a shaggy, thick, yellow membrane, gangrenous and stinking, which completely hides the subjacent mucosa except for a narrow strip in front, running up for about 2½ inches from the bifurcation.

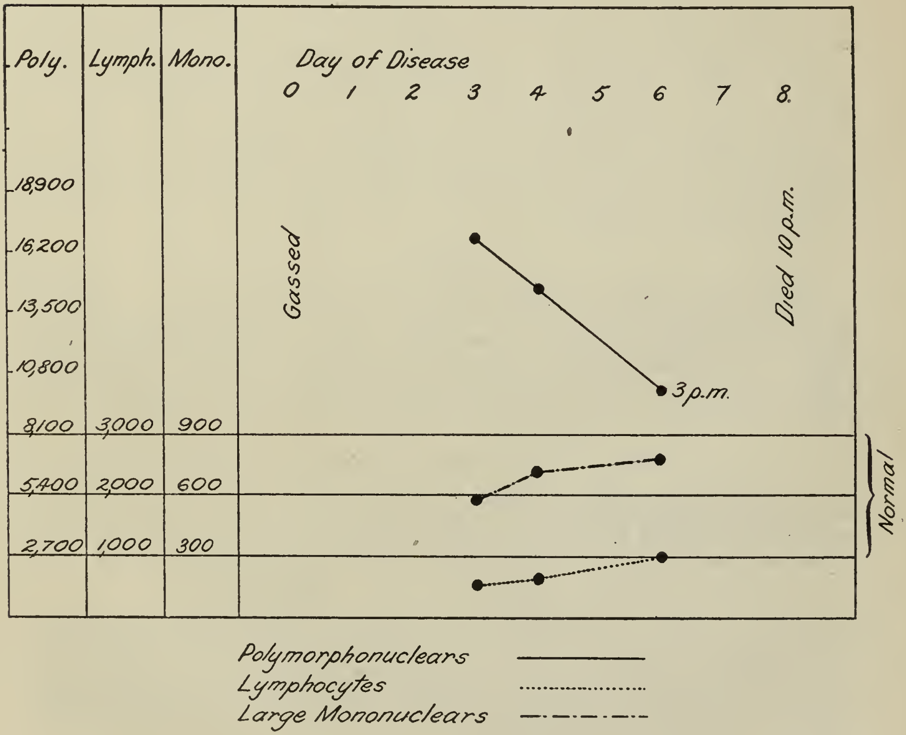
3. *Lungs and Pleuræ.*—The gangrenous bronchitis seen in the main tubes is found to extend to those of middle size at least. The smallest visible bronchi appear to contain pus as well as membrane, and round them are numerous patches of well-marked broncho-pneumonia. These areas are irregularly scattered throughout both lungs, being most numerous and most marked in the lower lobes. The consolidated areas show points of well-marked suppurative softening, patches of greyish-yellow consolidation, and areas of intense engorgement and hæmorrhage. The intervening non-consolidated portions of lung tissue, few and small in the lower lobes, more abundant in the upper, are intensely œdematous. The anterior marginal region of both lungs show well-marked interstitial emphysema. There is acute pleurisy with a small amount of plastic effusion and innumerable points of hæmorrhage over the whole of both lungs except the apical portions.

4. *Other organs.*—The right lobe of the thyroid is enlarged to six or eight times its normal size, and shows on section a number of soft, fleshy adenomata, with some which are necrotic and others cystic in the centre. The left lobe is two or three times the normal size, a parenchymatous hyperplasia chiefly, with a few small adenomata. The visceral pericardium shows much chronic fibrous thickening. The heart, which is otherwise normal, contains tough, white ante-mortem coagula in all chambers. There are some patches of hæmorrhage into the parietal peritoneum. The spleen is slightly enlarged, dark and very soft. The adrenals are of normal size, but the cortex is almost totally lacking in lipoid. The small vessels of the brain are intensely engorged.

Case 10.

Pte. W. was gassed on 12th October and admitted to No. —— Field Ambulance the same day suffering from sore throat and sore eyes, coughing and vomiting. Next day he was admitted to No. —— C.C.S., when there was conjunctivitis with great œdema, and pain in the throat and chest. The lungs and heart were apparently normal, the temperature was 98°, the pulse 80. On 14th October he was admitted to No. —— General Hospital, and the following day was very ill, cyanosed and aphonic, with copious purulent expectoration. A blood examination at 1 p.m. showed total leucocytes 18,000, neutrophils 16,920 (94 per cent.), eosinophils 0, basophils 0, lymphocytes 500 (2·8 per cent.), and large mononuclears 580 (3·2 per cent.). An examination on 16th October at 4 p.m. showed total leucocytes 16,000, neutrophils 14,660, eosinophils and basophils 0, lymphocytes 640 (4 per cent.), and large mononuclears 700 (4·4 per cent.). A third blood count, at 3.30 p.m. on 18th October, showed total leucocytes 12,000, neutrophils 10,200 (85 per cent.), eosinophils and basophils each 20 (0·2 per cent.), lymphocytes 980 (8·2 per cent.), and large mono-

CHART 5.—*Case* 10. Pte. W.



nuclears 780 (6·4 per cent.). The patient thereafter went steadily down hill, with a rapidly developing purulent bronchitis. He died at 10 p.m. on 20th October, eight days after gassing.

Post-mortem Examination (12 *hours after death*).

1. *External Appearances.*—There is a slight purulent conjunctivitis and superficial keratitis. There is a hæmorrhagic, scabby condition around the mouth and nostrils.

2. *Respiratory Passages.*—There is well-marked acute membranous inflammation of the pharynx, epiglottis, soft palate and uvula, the membrane being thick, white and firmly adherent. The larynx, trachea, and bronchi are the seat of a similar lesion, but the membrane is much thicker and less firmly adherent, especially over the front of the trachea and bronchi, where it is easily washed away. The mucosa beneath is intensely injected, with fine points of hæmorrhage.

3. *Lungs and Pleuræ.*—There is very extreme purulent bronchitis of the middle-sized and smaller tubes, from which much thick, yellow, creamy pus exudes on pressure. In the larger bronchi the inflammatory lesion is essentially membranous and there is less fluid pus. There is very widespread early broncho-pneumonia, most advanced and most extensive in the right upper lobe, but present everywhere throughout both lungs. There is an early acute pleurisy on both sides, with a small amount of plastic exudation and numerous punctiform hæmorrhages over the posterior aspect of the lower lobes especially.

4. *Other Organs.*—The tracheal and bronchial glands are very greatly enlarged and engorged. The adrenals are fairly rich in cortical lipoid. The brain shows intense engorgement of the smaller vessels, but is otherwise normal. The gastric mucosa is largely clothed with a thick layer of greenish mucopus.

C.—DESCRIPTION OF THE HISTOLOGICAL CHANGES.

1. *The Respiratory System.*

A large number of blocks were taken from various parts of the respiratory system, from the trachea, bronchi and bronchioles in every case; and from the nasal septum, uvula, pharynx, epiglottis and larynx in several. The lung changes were investigated in each case in a series of blocks taken from parts which showed different appearances to the naked eye.

It may be stated at once that all ten cases show very similar changes throughout the respiratory tract. They differ from one another only in respect of the severity or degree of the lesions present, and it cannot be said that this is demonstrably related to the duration of the disease (*i.e.*, to the number of days intervening between the time of gassing and the fatal issue), except possibly as regards gangrenous changes in the bronchi and lungs. All the cases belong to the rapidly fatal group, *i.e.*, all died within two to eight days of gassing. The writer has had no experience of cases dying at a later date. It seems reasonable to suppose that the variations in severity depend rather on the duration of exposure to the gas or on the degree of concentration of the latter, or both, but no data are here available on which to decide this point.

The respiratory changes are seen in their least advanced form in Case 7, which is primarily and essentially a skin case. Here broncho-pneumonia is absent, though present in every one of the other nine cases.

(*a*) *Changes in the Respiratory Passages.*—Very similar lesions are present in the various parts of the respiratory tree from the nasopharynx to the bronchi. In general terms the lesion may be described as an acute membranous inflammation, with associated vascular and cellular changes of various kinds and degrees.

(1) The earliest change appears to be a simple vascular engorgement (Fig. 1), which persists throughout, until either the vessels become thrombosed, or the tissue becomes involved in a fibrinous-inflammatory or necrotic process. Capillaries, venules and veins are all involved, and in some cases the engorgement is so extreme that the mucosa comes to be merely a closely-set congeries of widely-dilated vessels, with or without an epithelial covering. The engorgement is occasionally associated with hæmorrhagic extravasation into the cellular tissues of the part, best seen, perhaps, in the walls of the medium and smaller bronchi (Fig. 2).

(2) Capillary and venous thrombosis ensue, especially in the superficial, sub-epithelial zone. The smaller vessels are seen to be blocked by dense plugs of fibrin, while in the veins and venules there is a more open, fibrinous meshwork. In some cases the vessels contain true hyaline thrombi, which do not give the staining reactions of fibrin, while other vessels are simply occupied by blood clot in which a fibrinous network encloses large numbers of red blood corpuscles. The oldest and densest thrombi invariably occur nearest the surface. When the inflammatory membrane is stripped from a portion of the mucosa in which all or most of the vessels are thrombosed, the tissue beneath is quite pale to the naked eye, instead of presenting the usual bright red colour.

(3) Epithelial disintegration and desquamation and the formation of an inflammatory membrane proceed *pari passu* in practically every case (Fig. 3). As in other varieties of membranous inflammation of the respiratory tract, the appearances differ according to whether the part is covered by stratified squamous or by ciliated columnar epithelium. In both, the membrane is composed of fibrinous exudation forming a reticulum of varying density, in the meshes of which are found living and dead leucocytes and epithelial cells, with large numbers of bacteria. The surface layers of the membrane, where most of the bacteria congregate, usually fail to take the fibrin stain, and are composed largely of granular débris. In the case of squamous surfaces like the pharynx the membrane merges gradually into the subjacent mucosa ; there is no sharp line of differentiation (Fig. 4). This explains why it is so firmly adherent at post-mortem. On squamous surfaces, also, the membrane is usually patchily distributed, and at the margins of such patches the normal epithelium simply thins out and disappears, its place being taken by the much thicker inflammatory membrane. In the case of surfaces normally clothed by ciliated columnar epithelium the membrane is, as a rule, softer and less densely fibrinous ; it is, in fact, often highly œdematous, consisting of a fine, loose, fibrinous reticulum, the interstices of which are ballooned out during life by fluid effusion containing neutrophil leucocytes in larger or smaller numbers. Such a membrane is in most cases separated from the subjacent living tissue by an intact

and well-defined basement membrane (Fig. 3), but when the lesion is more severe the latter may break up and disappear, and the condition comes to resemble that seen in the case of squamous epithelial surfaces. So long as the basement membrane remains, the inflammatory membrane can be separated from it with comparative ease, and in sections, such separation is often apparently taking place spontaneously. Sometimes a single interrupted layer of epithelial cells still remains between the two; sometimes, especially near the orifice of a mucous gland duct, the inflammatory membrane is separated from the basement membrane by a loose collection of epithelial cells and mucoid secretion. This appearance is also seen in connection with squamous epithelial surfaces. The thickness of the inflammatory membrane varies very much, and in the smaller bronchi and bronchioles may lead to very serious diminution in the calibre of the tube, or even to complete obstruction by a fibrinous or fibrino-purulent plug (Figs. 2 and 5). Not infrequently the fibrinous membrane comes to a stop in the larger or middle-sized bronchi, and the lumen of the smaller bronchi and bronchioles beyond may then either be quite empty, or contain varying quantities of fluid pus. This may or may not be associated with some degree of dilatation. The epithelium in these smaller bronchi and bronchioles is often still intact, even when the lumen is completely occupied by pus or by a fibrino-purulent plug (Fig. 2). More often the epithelial layer is itself infiltrated by leucocytes, and may show a rupture at one or more points, so that there is free communication between the pus in the bronchiole and that in the surrounding pneumonic patch. This is well seen in Fig. 6, where the rupture of the wall is allowing not only egress for the contained pus, but also ingress for carbon-filled phagocytes from an adjacent focus of anthracosis.

The number of leucocytes emmeshed in the inflammatory membrane varies greatly, and is in inverse ratio to the amount of fibrin. In general they are more abundant in the smaller tubes, while the most densely fibrinous membrane is usually found in the upper respiratory passages. In some of the less seriously affected parts, especially in the skin case above referred to, there is neither membrane formation nor epithelial desquamation, or the latter alone may be present. In the case of the pharynx, uvula, nasal septum and epiglottis, membrane formation is almost invariably patchy. On the nasal septum only a few small thin patches of membrane are present here and there. On the uvula the changes are most intense on the pharyngeal aspect; on the epiglottis, on the posterior surface and at the bottom of the valleculæ. In the larynx, epithelial desquamation and membrane formation are most marked on and below the true vocal chords (Fig. 4), to a somewhat less extent on and above the false vocal chords, while the ventricle is quite unaffected.

(4) The inflammatory membrane above described is invariably associated with a greater or less degree of fibrinous inflammation within the living mucosa and submucosa, and in many cases with similar changes in the surrounding cellular tissues. Slight degrees of this interstitial fibrinous inflammation may even be present before

any inflammatory membrane is formed on the surface. It is often accompanied by a moderate amount of polymorphic and lymphocytic infiltration, both focal and diffuse. Eosinophil cells in small numbers were found in one case only, and then only in the pharynx.

(5) Œdematous infiltration of the mucosa and submucosa is found in the uvula and larynx, especially in the false vocal chords, to a less extent in the trachea and bronchi. In several cases œdema of the glottis and of the posterior third of the tongue was noted at post-mortem, but was not investigated histologically. As already mentioned, the inflammatory membrane in the trachea and bronchi is sometimes ballooned out by dropsical effusion.

(6) The muscularis mucosæ of the trachea and bronchi may be practically unaltered in slighter cases; more often it is broken up by fibrinous inflammation and by the presence of engorged capillaries (Fig. 3). In the most severe cases, where the whole mucosa is greatly disorganised, it may be barely distinguishable, a mere collection of eosin-staining dots in the zone immediately beneath the basement membrane.

(7) The mucous glands show histological changes only in severe cases, when early necrosis and desquamation may be observed. Sometimes the stroma is infiltrated by lymphocytes and plasma cells. The ducts may be catarrhal, but often show no change. Often their orifices are occupied by short prolongations of the inflammatory membrane, and occasionally the membrane prevents the escape of the mucous secretion, which then collects between the inflammatory and basement membranes.

(8) Bacteria are invariably present in large numbers in the inflammatory membrane, especially in the larger air passages. Gram positive cocci have been demonstrated in all ten cases, Gram negative diplococci in seven, and Gram positive diphtheroid bacilli in five. *B. fusiformis* was present in one of the gangrenous cases. Of the Gram positive cocci present the most frequent was a short chained diplostreptococcus morphologically resembling the pneumococcus, which was found in eight of the cases. A streptococcus which formed very long chains was present in Case 1. Other Gram positive diplococci were seen in seven cases, staphylococci in four.

The distribution of the bacteria is striking. The Gram positive cocci in general are found everywhere in the inflammatory membrane, penetrating even into bronchioles which are completely plugged with exudate. Where there is a breach in the basement membrane they invade the walls of the trachea and bronchi to a slight extent, and in several cases they are found invading the pneumonic patches in the lungs. The Gram negative diplococci, on the other hand, are in every case confined to the surface layers of the inflammatory membrane, where they form enormous masses visible, in stained sections, even to the naked eye. They are rarely found in the bronchioles, and never in those which are filled with a plug of fibrinous exudate. They do not appear to invade the living tissues, either in lungs or in bronchi. The largest numbers of bacteria are found in Cases 8 and 9, where gangrenous changes are taking place in the lungs. Here the pus-filled bronchi and the gangrenous centres of the broncho-pneumonic patches show enormous numbers of organisms. (These observations on the bacteria are entirely histological; no cultures were taken.)

(*b*) *Changes in the Lungs.*—Certain circulatory and inflammatory changes are present to a greater or less degree in all ten cases, namely, vascular engorgement, œdema, and alveolar catarrh. Other changes are present in the great majority, namely, suppurative broncho-pneumonia, and intra-alveolar hæmorrhage in nine cases, fibrinous pneumonia in seven. Actual gangrene of the lung is present in two cases only (Nos. 8 and 9).

(i) Suppurative Broncho-pneumonia.—The only case where this is absent is No. 7, which is essentially a skin case. In four cases—Nos. 1, 2, 5 and 6—the lesion is a comparatively slight one, small collections of pus-filled alveoli usually occurring in relation to small pus-filled bronchioles. In the other five cases the lesion is more advanced, and is associated here and there with actual breaking-down of the alveolar walls, best seen in Cases 8 and 9, where there is an associated gangrenous condition. In two cases—Nos. 3 and 4—there are large areas of confluent broncho-pneumonia, limited in Case 3 to the right middle lobe, in Case 4 to the right upper lobe. Here also the alveolar walls are disintegrating; the lesion is progressing from a state of red and grey hepatisation to one of diffuse suppurative softening. In the more advanced cases especially, the walls of the bronchioles are frequently ruptured at one or more points (Fig. 6); in the most extreme instances they are almost completely disorganised and barely recognisable as bronchial tubes at all. These broncho-pneumonic lesions are confined, in the slighter cases, to the posterior portions of the lower lobes, but in the advanced cases they are more generally or more irregularly distributed.

(ii) Fibrinous Pneumonia (Figs. 7 and 8).—This is notably present in all the five severe cases—Nos. 3, 4, 8, 9 and 10—and to a slight extent in Cases 1 and 5. The affected areas are rather irregularly scattered, but tend to occur around those medium-sized and smaller bronchi which are the seat of intense membranous inflammation, while bearing no relationship to pus-filled bronchioles or their associated patches of suppurative broncho-pneumonia. In Cases 3 and 4, where large confluent areas of pneumonic consolidation occur, and in the cases associated with gangrene (Nos. 8 and 9), the pneumonic lesions are partly purulent, partly fibrinous. For the rest, the two types of inflammation appear to remain separate, the one related to pus-filled bronchioles, the other surrounding larger tubes lined by a fibrinous inflammatory membrane. In these areas of fibrinous pneumonia there is often widespread thrombosis of the capillaries and venules in the alveolar walls.

(iii) Alveolar Catarrh (Fig. 9).—This is even more widespread than either of the foregoing, with both of which it is very commonly associated. There are all grades of severity, from slightly affected alveoli in which a few swollen desquamated epithelial cells lie free in the lumen, to those in which this space is completely occupied by these cast-off cells. Similarly, there are all gradations from a simple catarrhal desquamation to lesions in which polymorphonuclear leucocytes predominate, and this is often well seen at the margins of broncho-pneumonic patches. Varying numbers of red blood corpuscles may also be present. The great majority of the desquamated alveolar cells contain varying amounts of greenish-brown pigment.

(iv) Œdema (Figs. 10, 11 and 12).—Like the last mentioned, this change is present in all ten cases, though not always so strikingly as to be obvious to the naked eye. It is seen most frequently in relation to patches of broncho-pneumonic consolidation, where it occupies the intervening lung tissue, or at the margins of larger pneumonic areas (Fig. 10). Elsewhere it is unassociated with any such change, and shows then a tendency to lobar distribution. In Case 1, for example, the right upper lobe is extremely œdematous, while the rest of this lung and the whole of the left are practically free from œdema. The alveoli of the affected portions of lung contain a very finely granular, almost homogeneous material, deposited from the œdema fluid in the process of fixation. This may entirely fill the alveoli over considerable areas, or it may be present only at the periphery, the centre of the alveolus being occupied by a round or oval space. Generally, the œdematous portions of lung are also intensely engorged, and various combinations of œdema with catarrhal desquamation, leucocytic emigration and intra-alveolar hæmorrhage are frequently met with.

Œdematous infiltration of the septal and other connective tissues of the lung is also of common occurrence (Fig. 11), and extreme distension of the perivascular lymph channels can be made out in some of the cases (Fig. 12). Occasionally there is evidence of œdematous effusion into the lumen of the bronchi and bronchioles. Association of œdema with fibrinous inflammation is sometimes seen in all three situations, intra-alveolar, intra-bronchial and interstitial.

(v) Vascular Engorgement (Figs. 7, 10 and 13).—This is perhaps the most uniformly constant of all the pulmonary changes. The capillaries and venules of the alveolar walls and the larger vessels throughout the lungs are equally involved, while, as already mentioned, the bronchial walls and surrounding cellular tissues are often intensely affected. The only portions of lung which do not show capillary congestion are those areas of intense purulent or fibrinous pneumonia referred to above, where either the alveolar walls are undergoing a process of suppurative softening or the capillaries are blocked by fibrinous thrombi. Œdematous and catarrhal portions of lung, on the other hand, usually show the most intense vascular engorgement (Figs. 10 and 13).

(vi) Hæmorrhage (Figs. 2 and 14).—Various grades of intra-alveolar hæmorrhage are a common accompaniment of the vascular congestion. In the slighter cases this is doubtless due to small escapes of red cells (per diapedesin or per rhexin) from the engorged and often varicose capillaries. In more severe cases a condition of actual hæmorrhagic infarction obtains, the alveoli being stuffed with recent clotted or unclotted blood, while the alveolar walls show more or less necrosis and disorganisation. A thrombosed vein of larger or smaller size can often be demonstrated in immediate relationship to such an infarct. Areas of gross interstitial hæmorrhage occur with some frequency, and a hæmorrhagic zone of considerable breadth is often present around intensely inflamed bronchi and bronchioles, particularly the latter (Fig. 2). There is also considerable hæmorrhage into the alveolar walls themselves, with or without extravasation into the lumen.

(vii) Emphysema.—This is not a conspicuous feature, even in cases where broncho-pneumonia is well marked. A few emphysematous patches are found here and there in certain cases.

(viii) Collapse.—Small areas of recent collapse are seen here and there in most of the cases, usually in relation to patches of broncho-pneumonic consolidation. The epithelial lining of these collapsed alveoli is often much better preserved than that of the lung generally, and the cells may be cubical or sub-columnar.

(ix) Gangrene.—Gangrenous changes are present in the lungs in two cases only (Nos. 8 and 9), and then only in an early stage. These cases are characterised by the presence of small gangrenous cavities in the centre of the pneumonic areas, and in one case where a gangrenous tracheo-bronchitis also existed, by dilatation of the affected bronchioles. Such cavities, bronchial and pulmonary, are lined by a necrotic layer of varying width in which bacteria are present in enormous numbers, cocci, both Gram positive and Gram negative, diphtheroid bacilli, and in one case (No. 8) *B. fusiformis.*

(x) Bacteria.—Apart from the gangrenous cases just referred to, bacterial invasion of lung tissue occurs only in the central areas of the more advanced broncho-pneumonic patches, and is restricted to the Gram positive cocci. Even these are present only in quite small numbers. There is no evidence of any general or widespread invasion of the lung, even in the advanced pneumonic areas.

2. *Other Organs.*

(*a*) *The bronchial* and to a less extent *the tracheal lymph glands* are increased in size and the seat of intense engorgement in half the cases (Fig. 15). Microscopically, in addition to the vascular engorgement, there is evidence here and there of actual hæmorrhage into the lymph channels. In each case the lymphoid tissue is much reduced, and the lymph paths correspondingly increased in size, with evidence of active endothelial proliferation therein. Varying quantities of carbon are present.

(*b*) *The brain* was examined microscopically in six cases, all of which show intense capillary and venular engorgement, while in five of them hæmorrhages are present in the white matter. The latter are invariably of quite small size, a narrow ring of blood encircling the affected vessel, the wall of which usually consists of little more than a single layer of endothelial cells (Fig. 16). They are fairly circumscribed at the margin, presenting usually an oval or circular outline. The endothelium of some of the vessels presents a swollen, degenerate appearance, the cytoplasm taking the eosin strongly, while the nuclei barely stain at all. Others, especially where there is considerable extravasation of blood, contain numerous yellowish or brownish granules in their cytoplasm. Here and there thrombosis *in situ* may be observed (Fig. 17), and elsewhere small accumulations of neutrophil polymorphs are present in relation to some of the more degenerate endothelial tubes.

(*c*) *The adrenals* were examined microscopically in six cases. The most constant change, present in all of them, is intense engorgement of the innermost third or so of the cortex, including the zona-reticularis and part of the zona-fasciculata, with varying grades of engorgement of the adjacent outer zone of the medulla (Fig. 18). This is associated in Case 9 with a number of small focal hæmorrhages in the cortex, and in Case 8 with some focal round-cell accumulation.

(*d*) *The kidneys* were examined microscopically in six cases. All show a certain amount of congestion, chiefly of the medulla and glomeruli, and two show also cloudy swelling of the convoluted tubules.

(*e*) *The liver* was examined in nine cases, of which five show well-marked cloudy swelling, six varying grades of congestion, and three slight fatty change, characterised by the presence of a small number of large fat-vacuoles, chiefly at the periphery of the lobules. In one case there is extensive focal necrosis both in liver and kidneys, the result of a terminal Welch infection. One case shows early portal cirrhosis, and another a well-marked capsular cirrhosis.

(*f*) *The spleen* is engorged and slightly enlarged in six cases. In four of these which were examined microscopically, the engorgement of the pulp is intense, and is associated with a certain amount of focal hæmorrhage.

(*g*) In four cases in which *the myocardium* was examined, three are normal and one shows slight interstitial fibrosis.

(*h*) In Cases 7 and 10 the *mucosa of the pyloric half of the stomach* is covered by a thick layer of tenaceous greenish mucopus. Microscopically this is found to consist of mucus, emmeshing numerous desquamated epithelial cells. Pus cells are absent.

D.—RÉSUMÉ OF MORBID ANATOMICAL CHANGES.

1. In nine out of the ten fatal cases examined the principal lesions are those involving the respiratory tract—namely, an acute membranous inflammation of the naso-pharynx, larynx, trachea and bronchi; with the following lung changes, which vary in extent and in degree in different cases—namely, vascular engorgement, œdema, suppurative broncho-pneumonia, alveolar catarrh and intra-alveolar hæmorrhage.

2. In seven cases larger or smaller areas of fibrinous pneumonia are also present.

3. In two cases which died at the end of seven and eight days respectively, the broncho-pneumonia is very advanced, with actual gangrene and breaking-down of lung tissue. In one of them the membranous lesion in the trachea and bronchi is also become gangrenous.

4. In the respiratory cases bacteria of various sorts, especially

Gram positive cocci, are invariably present in large numbers in the inflammatory membrane and in the pus-containing bronchi and bronchioles. The lung tissue, however, is not invaded except in three cases, including the two cases of severe broncho-pneumonia with gangrene referred to above, in which the number of bacteria is enormous.

5. In Case 7 the extensive skin burns, which are almost universal, constitute the principal lesion. Neither broncho-pneumonia nor membranous tracheo-bronchitis are present, but the lungs show intense vascular engorgement, with intra-alveolar hæmorrhage, œdema and catarrh.

6. In only two of the respiratory cases is blistering of the skin absent.

7. Acute conjunctivitis and chemosis in varying degree are present in every case, superficial keratitis in half the cases.

8. Small punctiform hæmorrhages are present in the white matter of the cerebral hemispheres in five out of six cases examined.

9. Vascular engorgement of the adrenals, bronchial glands, spleen, liver and kidneys, sometimes accompanied in the case of the first three by focal hæmorrhages, is present in a certain proportion of cases. Cloudy swelling of the liver and kidneys is also present in some instances.

TABLE SHOWING THE FREQUENCY OF OCCURRENCE AND COMPARATIVE SEVERITY OF THE VARIOUS LUNG CHANGES.

Case.	Duration in days.	Œdema.	Suppurative broncho-pneumonia.	Fibrinous pneumonia.	Alveolar hæmorrhage.	Vascular engorgement.	Gangrene.	Catarrh.
1	2	++	+	+	++	++	—	++
2	2	+	+	—	+	+	—	++
3	3	+	+++*	++	+	++	—	+
4	5	+++	+++†	++	++	+	—	+
5	5	+	+	+	+++	+++	—	+
6	6	+++	+	—	++	++	—	++
7	7	+	—	—	++	++	—	++
8	7	++	+++	++	++	++	+	++
9	8	++	+++	++	++	++	+	++
10	8	++	++	++	—	++	—	++

* Confluent pneumonia, right middle lobe.
† Confluent pneumonia, right upper lobe.

E.—DESCRIPTION OF THE LEUCOCYTIC CHANGES.

The blood was examined in six out of the ten fatal cases, in one case once only, in one case twice, in three cases three times, and in one four times. In each, a remarkably constant and striking series of leucocytic changes was discovered, which may be summarised as follows :—

In the early stages—that is, from the first to the third day after gassing, occasionally later—there is usually a great increase in the total leucocyte count. This is fully accounted for by a large increase, relative and absolute, of the neutrophil polymorphs. The condition is well seen in Case 7 (Chart 3), where, on the second day after gassing, the total leucocyte count was 35,000, of which 33,800 (96·6 per cent.) were neutrophil polymorphs; or in Case 5 (Chart 1), where on the first day the total leucocyte count was 32,000, of which nearly 30,000 (93·3 per cent.) were neutrophils. Even where the total leucocyte count is not raised there is a striking relative neutrophilia. For example, in Case 8 (Chart 4), on the second day there were 8,000 leucocytes, of which 95·4 per cent. were neutrophil polymorphs. At the same time there is either a moderate or a great reduction in the number of lymphocytes, while the eosinophil and basophil cells practically disappear. The large mononuclear cells are either reduced or remain about normal, but in one case (Case 5), they were increased to about double the normal figure (Chart 1).

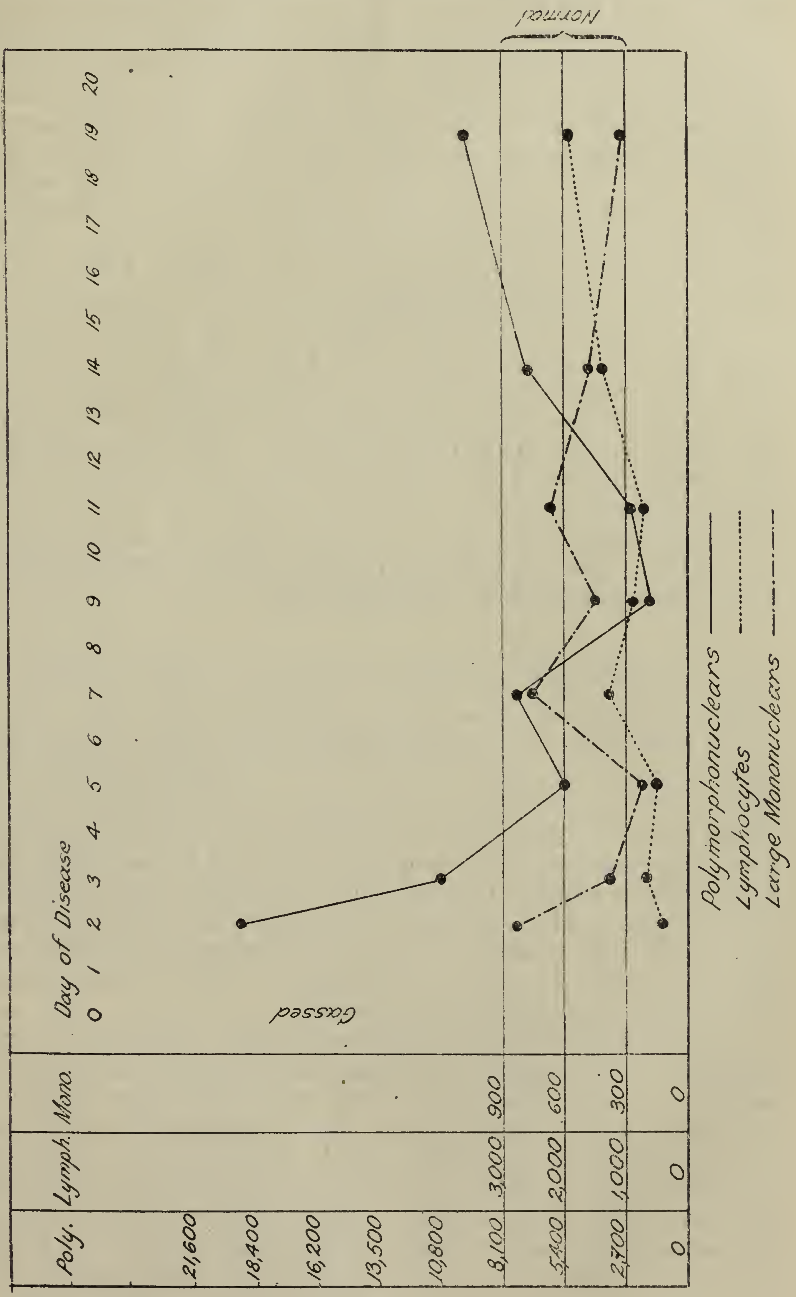
As the disease progresses towards a fatal issue (and in some very severe, non-fatal cases also), there occurs a rapid fall in the total and neutrophil counts, usually commencing about the third or fourth day, and reaching in the last day or two an excessively low figure indeed. In Case 7, for example (Chart 3), the neutrophils fell from 33,800 on the second day to 15,800 on the third, and to 172 on the seventh, six hours before death. In Case 6 (Chart 2) they fell from 14,370 on the third day to 2,670 on the sixth, four hours before death. In Case 8 (Chart 4) they fell from 7,630 on the second day to 6,650 on the third, 1,150 on the fifth and 270 on the sixth, exactly 24 hours before death. In one case only (Case 1), which died two days and nine hours after gassing, a terminal leucopænia was not observed. Here the total count six hours before death was 18,000, of which 16,500 (92 per cent.) were neutrophil polymorphs. Unfortunately this was the only count made in this case, and it is reasonable to suppose that a higher leucocytosis had existed at an earlier stage. The fall in neutrophils is accompanied by a further but much less striking reduction in the number of lymphocytes and large mononuclear cells, although, of course, these cells are relatively more abundant than in the earlier stages.

In three of the cases eosinophils and basophils were completely absent throughout, in the other three they were very greatly reduced.

These observations were confirmed, as regards the neutrophil changes, by a series of blood counts made in a case of severe mustard gas poisoning which recovered (Pte. H., Chart 6). Here on the second day the total leucocytes numbered 21,000, of which 19,700 (94 per cent.) were neutrophil polymorphs; eosinophils and basophils were absent, the lymphocytes numbered 420 (2 per cent.), while the large mononuclears were 840 (4 per cent.). By the fifth day the total count had fallen to 6,000, of which 5,200 (87·2 per cent.) were neutrophils; and by the ninth day, when the patient was about his worst, it was down to 3,100, with neutrophils only 1,700 (54·8 per cent.). The total and polymorph counts rose slowly thereafter as the patient recovered, until when he was evacuated to England on the 18th day there were 12,000 leucocytes, with 81·2 per cent. of neutrophils.

An interesting point observed in connection with the neutrophils

CHART 6· Pte. H.



is that while the general tendency was toward an embryonic type of nucleus, three and two lobes being the rule, quite a number of very large polymorphs containing nuclei with from six to eight lobes were met with in most cases. On the other hand, while metamyelocytes with kidney-shaped nuclei were not uncommon, true myelocytes were distinctly rare.

An interesting contrast to these severe and fatal cases is afforded by the case of Pte. S., who was never seriously ill, and who was well on the way to recovery when evacuated to England. He was gassed at the same time as most of the others, namely, October 12th, and he suffered from moderate laryngitis and conjunctivitis, but was without skin involvement save a large patch of brownish pigmentation on the right arm and shoulder. His blood was examined on four occasions, October 14th, 16th, 19th and 22nd. The total count varied between 12,000 and 9,600, the polymorphs between 8,000 and 4,700 (68 per cent. and 49 per cent.). The most striking change was an increase in the number of eosinophils, which varied between 1,250 and 870 per cub. mm. (Highest and lowest percentages 12·8 and 7·6.)

In six other slight cases of mustard gas poisoning in which the leucocytes were examined within a few days of gassing the average total count was 9,700, while the eosinophils were 380 per cub. mm., *i.e.*, at or above the upper limit of the normal for these cells. In one case there were 830 eosinophils per cub. mm. The other leucocytes were present in about their normal proportions, the average percentage of polymorphs being 60.

Red cell and hæmoglobin estimations were not carried out, but stained films showed the former to present a quite normal appearance, and the colour of the blood was always good.

F.—RÉSUMÉ AND DISCUSSION OF THE LEUCOCYTIC CHANGES.

The high neutrophil leucocytosis occurring in the early stages of severe mustard gas poisoning (from the first to the third or fourth day), while possibly dependent in part on the direct local action of the irritant, is probably chiefly the result of the secondary bacterial invasion of the damaged tissues which invariably ensues. At the same time, local leucocytosis is seen not merely in certain of the respiratory tract lesions where bacteria (pneumococci, streptococci, &c.) are present in very large numbers, but also in fluid from the vesicles, where no bacteria are seen in smears. It is also of interest to note that a very high neutrophilia is present in the skin case, No. 7, where the respiratory lesions are comparatively slight.

A rapid fall in the total number of hæmic leucocytes and more especially in the number of neutrophil polymorphs takes place, in severe cases, about the fourth or fifth day, occasionally earlier. In the worst cases the leucocytes may almost disappear from the blood, even as long as 24 hours before death. This rapidly developed and extreme leucopænia is clearly due to an acute failure of the leucoblastic function of the bone marrow, without, however, any associated erythroblastic failure. A similar phenomenon, leucoblastic without erythroblastic failure, but developing much more slowly, had previously been observed by the writer in certain cases of toxic jaundice due to trinitrotoluene.* It was thought at first that the rapid disappearance of the leucocytes from the circulating blood during the final stages might be related to the almost constant presence of large, white, ante-mortem coagula in the chambers of the heart. This, however, can only be a subsidiary factor, though it may help to account for the final, almost complete leucocytic depletion which takes place. It may be noted here that in the case of Pte. H. (Chart 6), who recovered, the lowest total leucocyte count was 3,100, while in two of the fatal cases the count fell to 500 and 200 respectively. The resemblance in respect of many of these features to severe and fatal cases of croupous pneumonia is remarkable, and is commented on below.

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* Stewart: Proceed. Roy. Soc. Med., 1917, Vol. X (March), pp. 10–36.

In the very severe cases the eosinophils become greatly reduced, and may even disappear, but in slight and moderately severe cases they tend to be increased, sometimes markedly so. These facts are clearly related to certain histological observations. In the above recorded ten fatal cases eosinophils were entirely absent from the local lesions, both respiratory and cutaneous, save for a very few, confined to the pharyngeal mucosa, in one case. On the other hand Edkins and Tweedy,* in their experimental work on rabbits, frequently observed a well-marked local eosinophilia in the respiratory lesions about the third or fourth day, only, however, in animals to whom a sublethal dose of gas had been administered. A similar reduction or actual disappearance of eosinophils is, of course, a well-known accompaniment of the neutrophil leucocytosis of acute lobar pneumonia, and it may be noted that all the mustard gas cases in which an eosinophil leucopænia was observed, showed, at least in the early stages, a concomitant absolute or relative neutrophilia of high degree. In other respects the leucocytic changes in severe mustard gas poisoning closely resemble those seen in certain cases of croupous pneumonia, for example, a high leucocyte count giving place before death to a pronounced leucopænia.

From a consideration of the facts above detailed, especially the striking contrast between the slight and the severe cases of mustard gas poisoning in respect of the leucocytic changes, and the close resemblance between the latter and many severe and fatal cases of acute lobar pneumonia, it is suggested that the leucocytic changes in the latter group are largely or even predominantly the result of the secondary bacterial invasion of the respiratory tract which invariably takes place. Although no cultural examinations were made, either before or after death, the examination of sections showed that organisms having the morphological and staining characters of the pneumococcus were present in large numbers in eight out of ten fatal cases, while in one of the remaining two a long chained streptococcus was present. It may be noted also that it was precisely these organisms which had penetrated most deeply into the inflammatory membrane, and were actually invading the bronchial walls and lung tissue in some cases, while the gram negative cocci and other bacteria remained in the more superficial zone.

Case 7, which showed the leucocytic changes very strikingly (Chart 3), is exceptional in that the respiratory lesions were early and slight, viz., engorgement and early epithelial desquamation of the tracheo-bronchial mucosa, with only tiny shreds of inflammatory membrane, and pulmonary engorgement, œdema and catarrh. Bacteria were few in number, and no suppurative lesions were present. The skin lesions, on the other hand, were very severe and almost universally distributed, and there was intense conjunctivitis with corneal ulceration.

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* Reports of the Chemical Warfare Medical Committee, No. 2.

Prognostic Value of the Leucocyte Count in the Early Stages of Mustard Gas Poisoning.

The number of cases examined is too few to warrant the formulation of any very dogmatic generalisations, but the changes present were so striking that one is perhaps justified in drawing the following tentative conclusions.

1. A very high relative neutrophilia, 90 per cent. or upwards, with or without an increased total leucocyte count, indicates a bad prognosis. Of seven cases in which the neutrophil polymorphs were present in proportions varying between 92 per cent. and 99 per cent., six died, and the seventh was very seriously ill for some days. On the other hand a series of seven slight and moderately severe cases showed an average of 60 per cent. neutrophils, the highest figure being 68 per cent.
2. A bad prognosis is also indicated by a rapid fall in the total leucocyte count to an extremely low figure, this usually taking place between the third and sixth days.
3. Maintenance of a good eosinophil count or the appearance of an eosinophilia, relative and absolute, is a good prognostic indication, great reduction or total absence of these cells a bad.
4. In the present series of cases the leucocytic changes found merely confirmed an already fairly obvious prognosis, good or bad. It is possible that in other cases these changes may have real prognostic value, either in warning the physician that a case apparently slight or doing well may yet be a proper source of anxiety, or in showing that a patient whose outlook seems bad may still have elements of hope in his case. Further work is necessary to determine these points.

ADDITIONAL REMARKS.

1. In all severe cases of mustard gas poisoning, in view of the widespread and serious pulmonary lesions which rapidly develop, it is clear that from the point of view of treatment complete rest, bodily and mental, is the ideal to be aimed at. The administration of oxygen is also indicated, or failing that, as good a supply of fresh air as possible.
2. The serious embarrassment of the right heart which is seen in many cases is clearly due to the great vascular stasis and even thrombosis so strikingly present throughout the lungs. There would appear to be no objection from a pathological point of view to the use of bleeding for the relief of this condition.
3. The great importance of the secondary bacterial invasion of the respiratory tract in these severe cases is strongly insisted on.

Treatment by means of antiseptic inhalations and sprays, or even by actual intracheal injections, would seem to be indicated, while thorough oral and nasopharyngeal hygiene with a view to diminishing the risk of infection should be instituted at the earliest possible moment. Edkins and Tweedy have shown that local neutrophil leucocytosis may occur in the respiratory tract of animals dying within 24 hours of the administration of a minimum lethal dose of mustard gas, and that before there was any evidence of bacterial invasion. They conclude that there is a definite chemiotactic action on the part of the poison. The lesions in these animals were, however, very different from and much less advanced than those found in man.

4. The punctiform hæmorrhages in the white matter of the brain are doubtless due, as suggested by Mott,* for cases of gas poisoning in general, to hyaline thrombosis in the cerebral venules, capillaries or arterioles. This would be conduced to by the demonstrably degenerate condition of the endothelium of many of these vessels (Fig. 17) as well as by the stasis due to a failing circulation. Increased coagulability of the blood, shown by MacNee and Dunn to be present in early gassed cases, is also a possible factor in their production, especially when the fibrinous inflammatory lesions existing in the lungs and bronchi are taken into account. No observations were made on the actual coagulation time of the blood in the present series of cases.

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* Proceed. Roy. Soc. Med., 1917, Vol. X (May), Path. Sect., p. 73.

Fig. 1.—(*Case* 6.) Tip of epiglottis, showing intense vascular engorgement and slight leucocytic infiltration. The epithelium is quite intact.

Fig. 2.—(*Case* 8.) (Mallory's acid fuchsin, anilin blue, orange G stain.) Portion of a bronchiole, the lumen of which is completely plugged by dense fibrinous exudate. The wall shows extreme vascular engorgement, but the epithelium is still intact. The bronchiole is surrounded by a narrow zone of intensely hæmorrhagic lung tissue.

Fig. 3.—(*Case* 5.) Trachea, showing intense vascular engorgement, slight leucocytic infiltration, and replacement of the mucosal epithelium by a loose fibrinous inflammatory membrane which is separating at the line of the basement membrane. Some of the smaller superficial vessels are thrombosed and the muscularis mucosæ is much broken up.

Fig. 4.—(*Case* 6.) Margin of the true vocal chord. In the upper part the epithelium is still intact, and there is intense vascular engorgement underneath. In the lower part the epithelium is lacking and its place is taken by a broad fibrinous inflammatory membrane.

Fig. 5.—(*Case* 5.) Portion of a small bronchus, the lumen of which is completely occupied by a somewhat laminated fibrinous plug, while the epithelial lining is completely desquamated. There is intense engorgement of the bronchial wall outside the narrow inner necrotic zone. A small portion of cartilage and some mucous glands are seen.

Fig. 6.—(*Case* 6.) Pus-filled bronchiole in the centre of an anthracotic nodule. The wall has ruptured and the pus is escaping, while at the same time carbon-filled phagocytes are gaining an entrance to the tube. There is intense engorgement of the surrounding tissues.

Fig. 7.—(*Case* 8.) Portion of lung, the seat of early fibrinous pneumonia (red hepatisation). There is intense engorgement of the capillaries of the alveolar walls, with some diapedesis of red cells. The alveoli are filled with fibrinous plugs containing few cells.

Fig. 8.—(*Case* 8.) (Weigert's fibrin stain.) Portion of lung which is the seat of advanced fibrinous pneumonia. The fibrinous plugs filling the alveoli enclose varying numbers of red blood corpuscles and desquamated epithelial cells, but there is no engorgement of the alveolar walls, the vessels therein being thrombosed.

Fig. 9.—(*Case* 3.) Early alveolar catarrh. The lung alveoli contain small numbers of pigment-filled catarrhal cells and leucocytes, while their walls are more or less denuded of epithelium. There is a certain amount of congestion.

Fig. 10.—(*Case* 1.) Œdema of the lung. The alveoli are almost completely filled by œdematous effusion. A number of desquamated epithelial cells, many of them containing pigment granules, are also present. The capillaries of the alveolar walls are intensely engorged.

Fig. 11.—(*Case* 9.) Intense œdema of an interlobular septum of the lung. On one side there is a suppurative pneumonic lesion, on the other pulmonary œdema.

Fig. 12.—(*Case* 9.) Portion of the wall of a radicle of the pulmonary vein, showing extreme dropsical distension of a perivascular lymph channel.

Fig. 13.—(*Case* 1.) (From a section stained by Mallory's acid fuchsin, anilin blue, orange G method.) Engorgement of the lung alveoli with epithelial desquamation. Many of the epithelial cells contain granules of pigment.

Fig. 14.—(*Case* 7.) Hæmorrhagic infarction of lung. There is great disorganisation of lung tissue and extreme hæmorrhagic infiltration.

Fig. 15.—(*Case* 6.) Bronchial gland showing intense vascular engorgement and early focal hæmorrhages. The number of endothelial cells is greatly increased and the lymphocytes correspondingly diminished.

Fig. 16.—(*Case* 5.) Punctiform hæmorrhage in the white matter of the brain (centrum ovale).

Fig. 17.—(*Case* 3.) Hyaline thrombosis of a cerebral capillary. The endothelial cells are swollen and degenerate.

Fig. 18.—(*Case* 8.) Adrenal cortex showing intense vascular engorgement and a certain amount of early necrosis and disintegration of the epithelial cell columns. These cells are also deficient in cortical lipoid.

The drawings are by Miss Ethel Wright, Leeds. All are from slides stained by hæmalum and eosin or hæmatoxylin and eosin unless where otherwise indicated.

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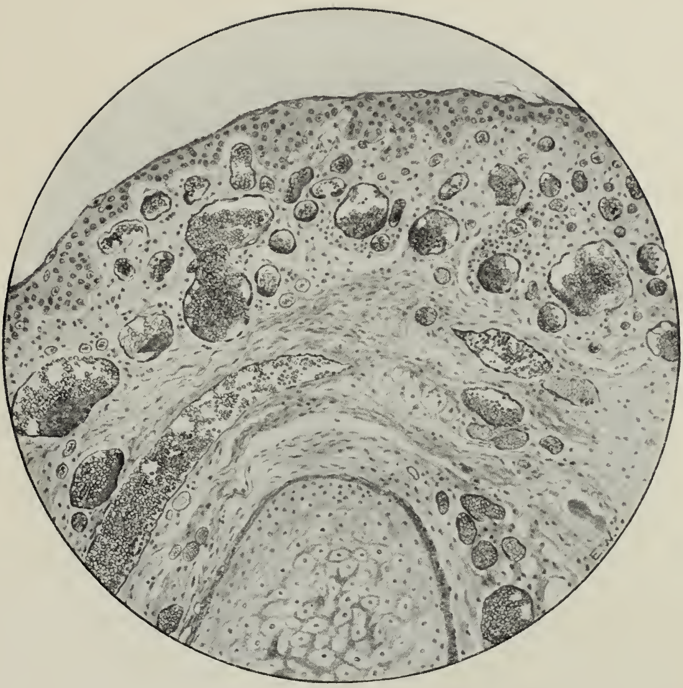

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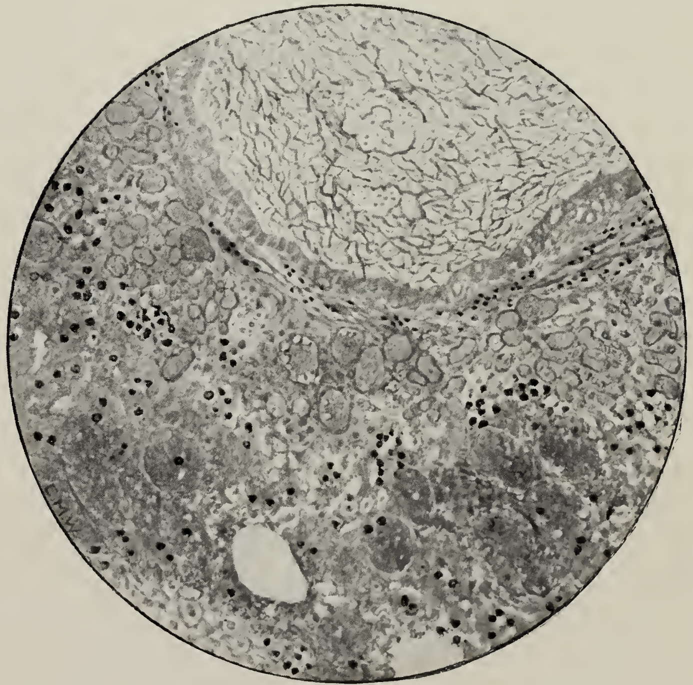

Fig 2.

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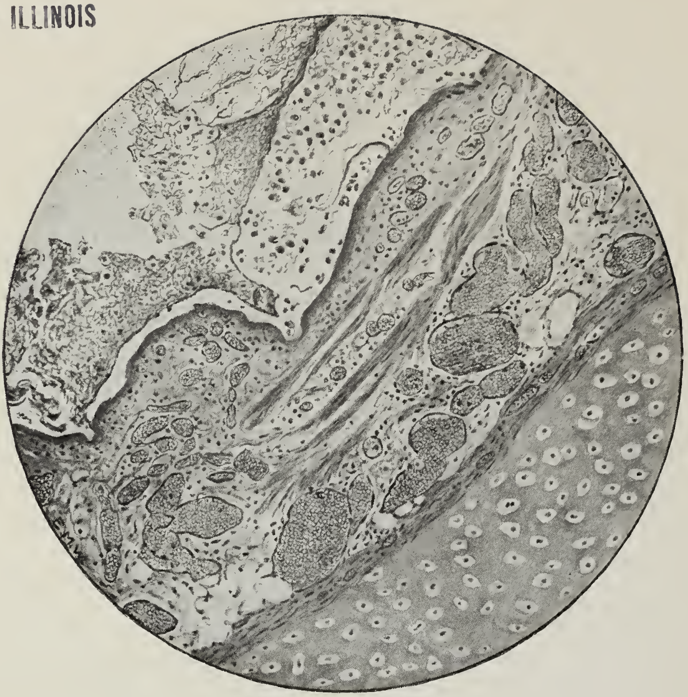

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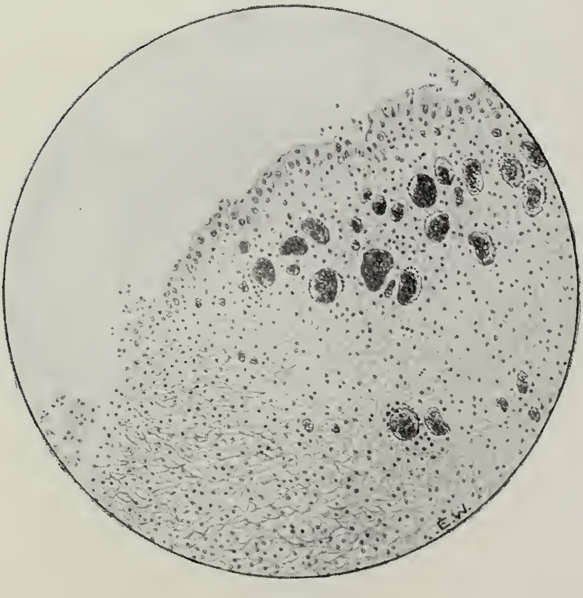

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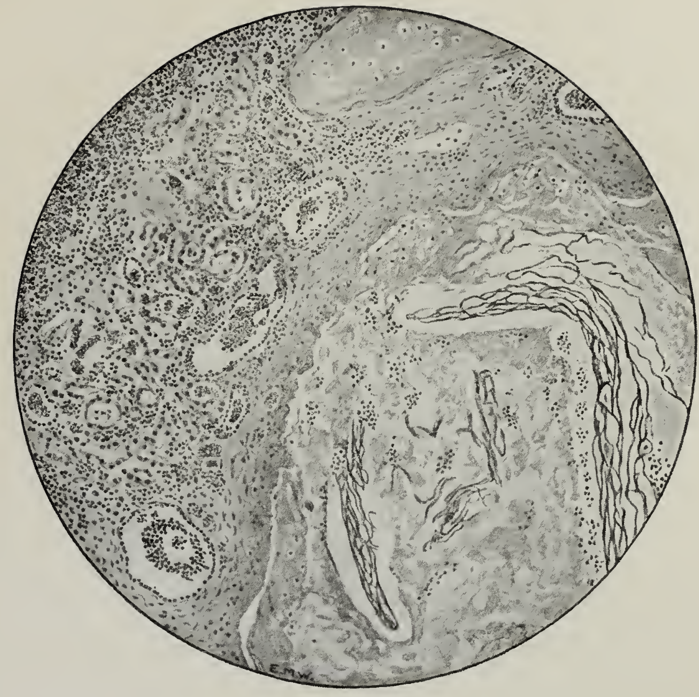

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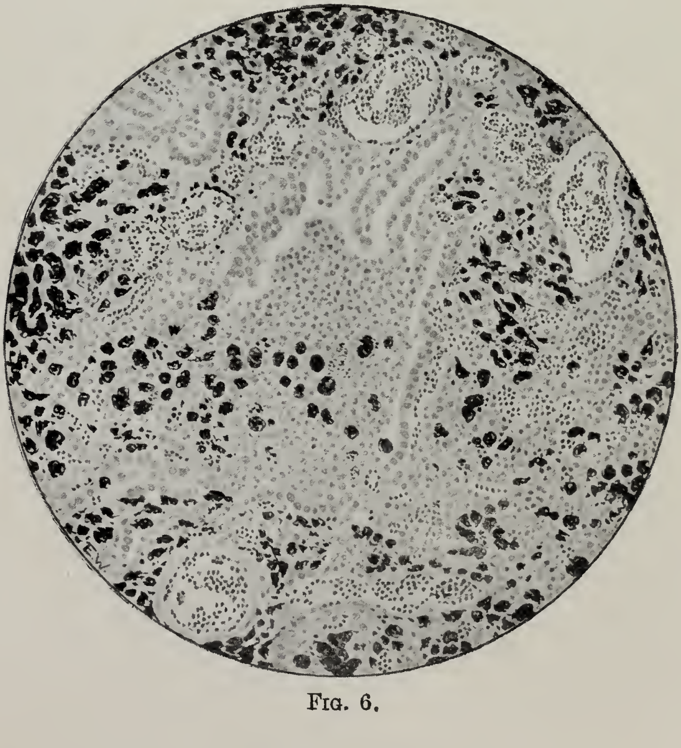

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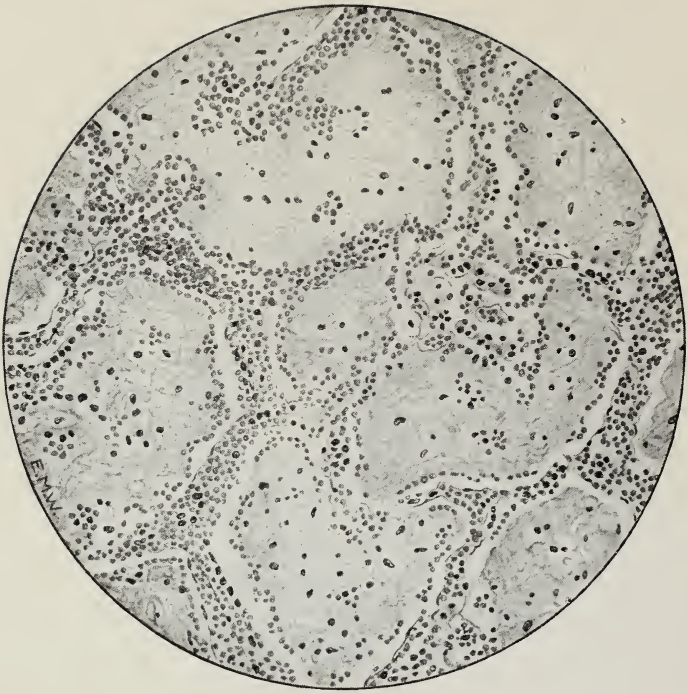

Fig. 7.

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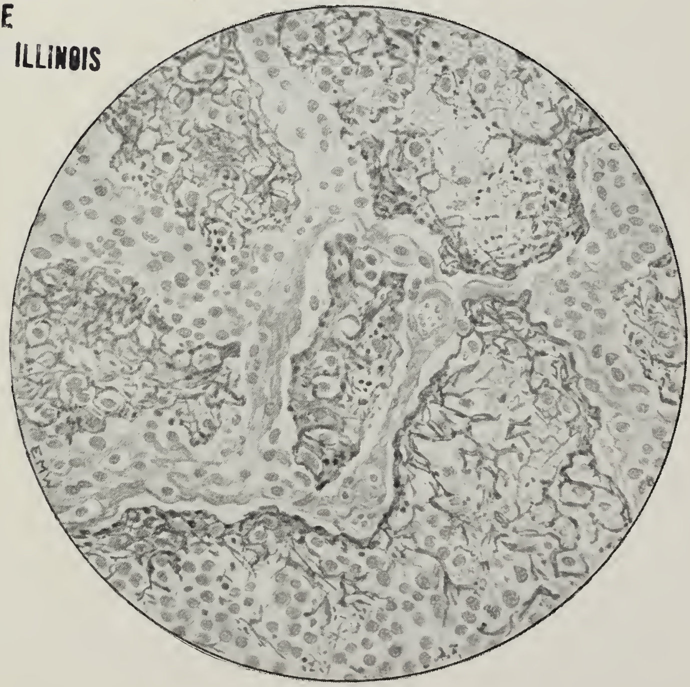

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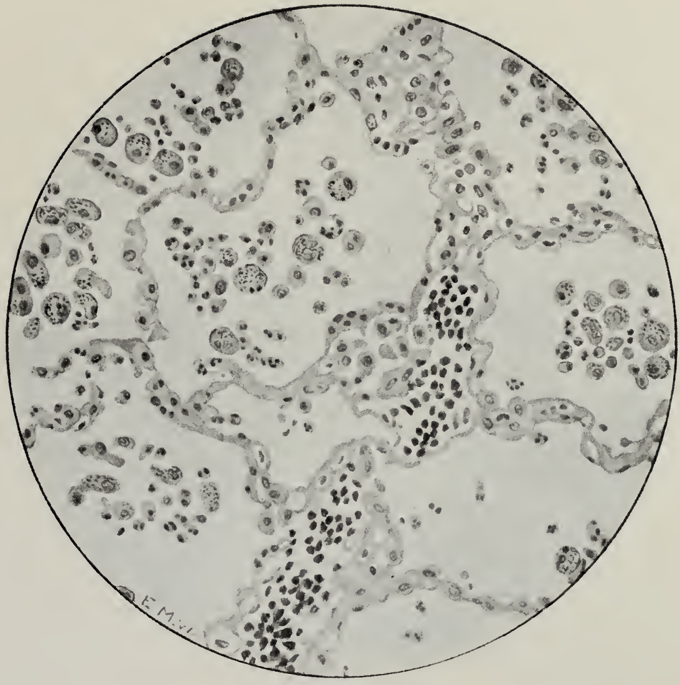

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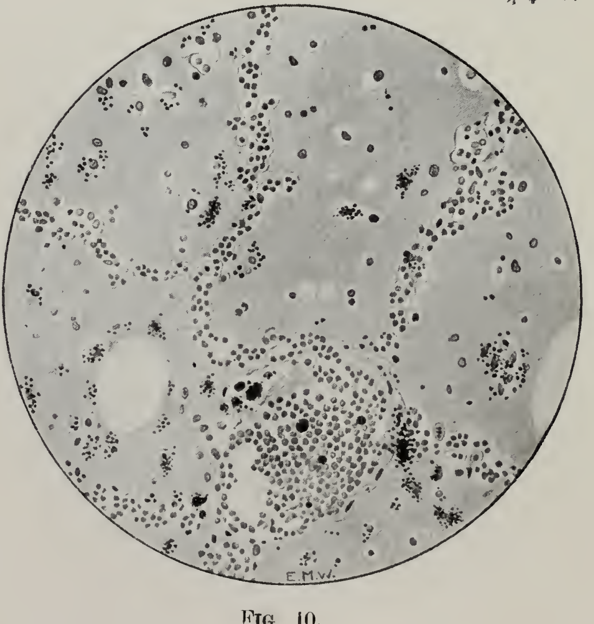

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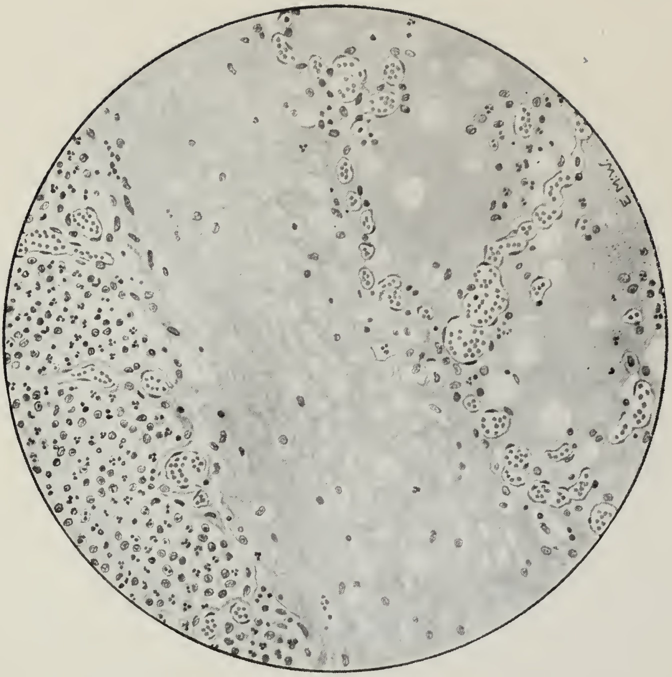

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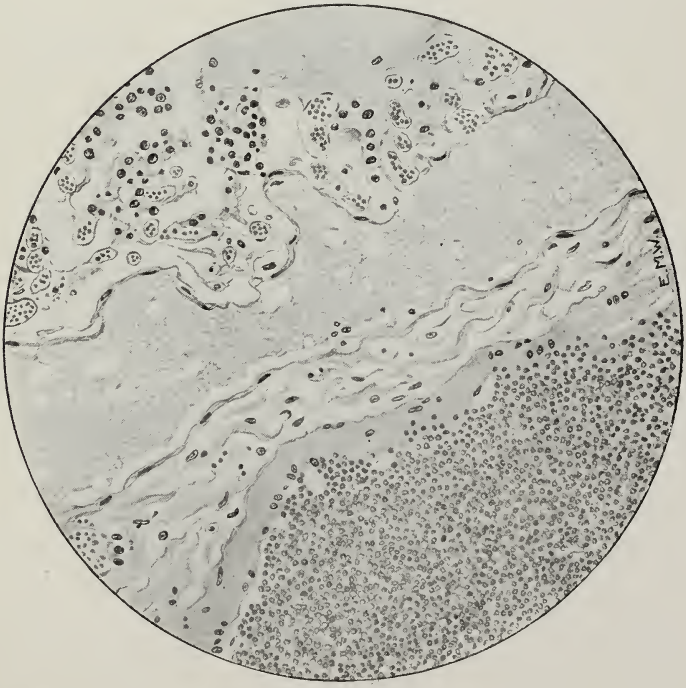

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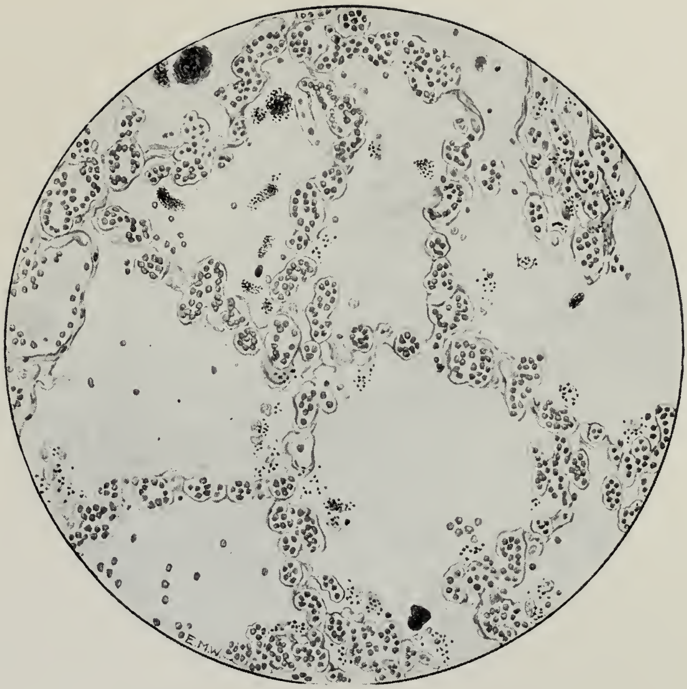

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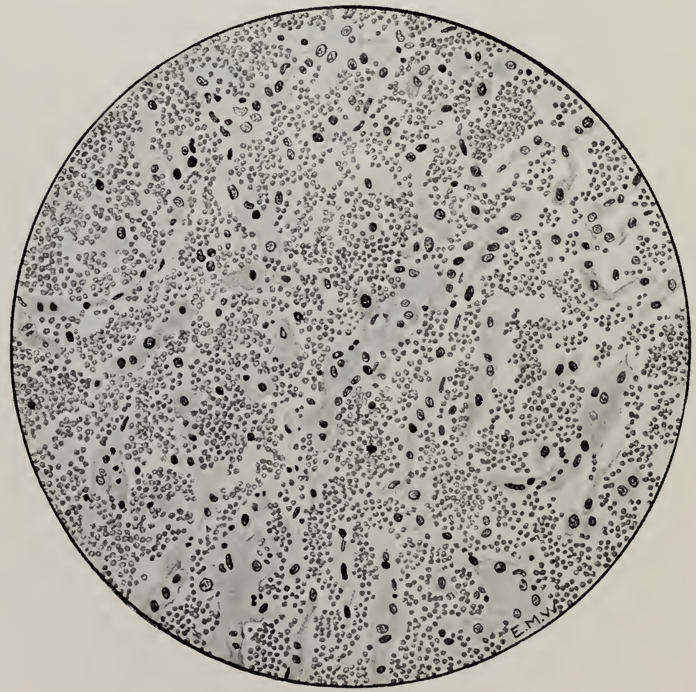

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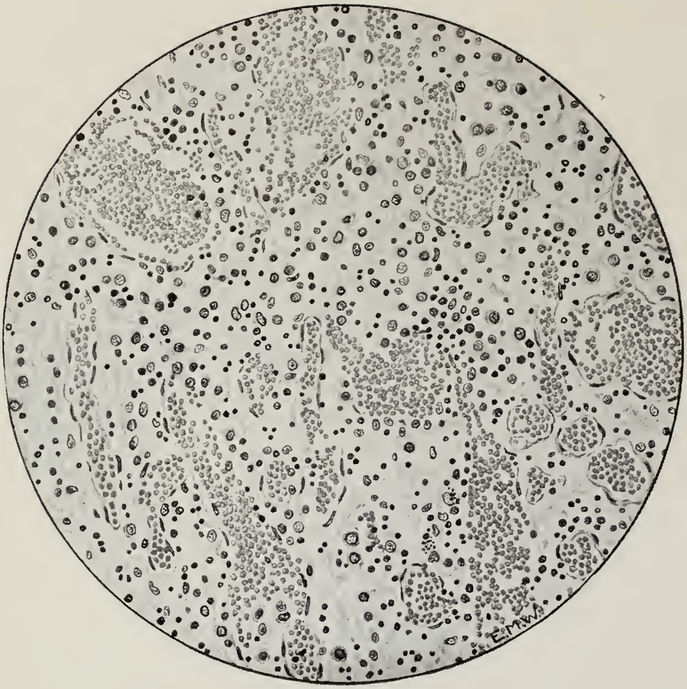

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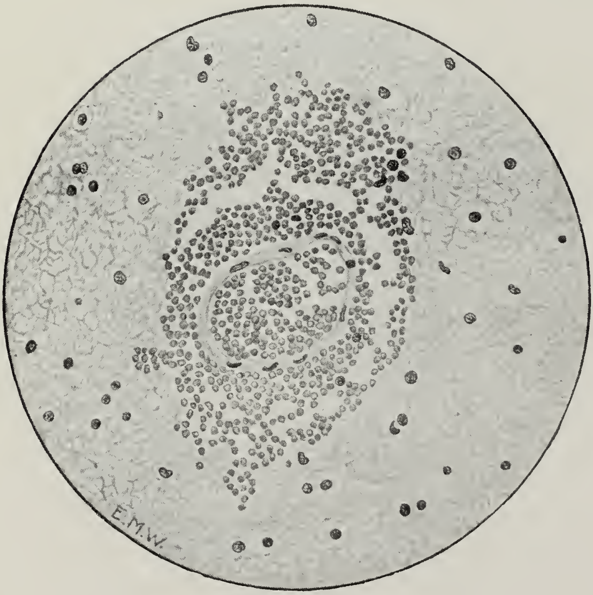

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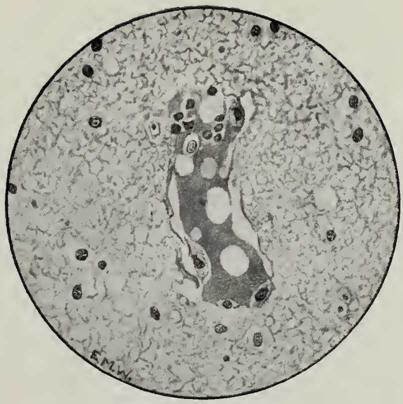

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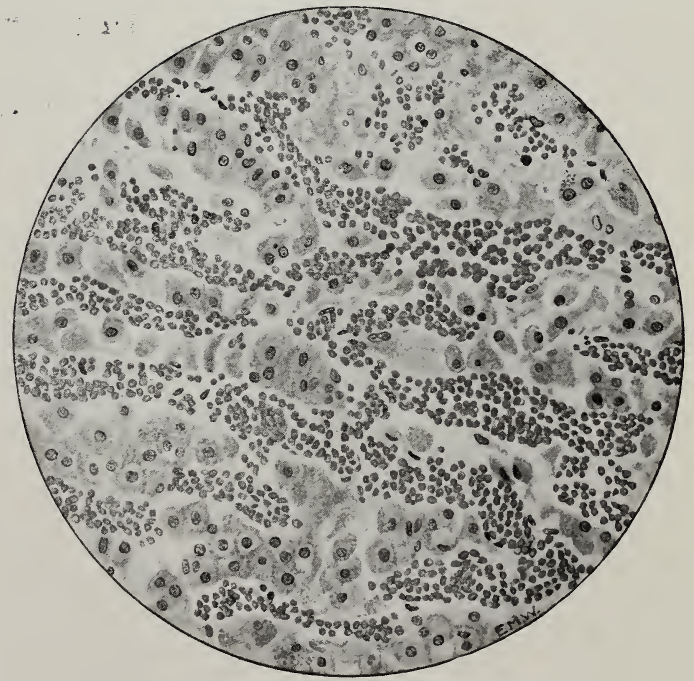

Fig. 18.

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